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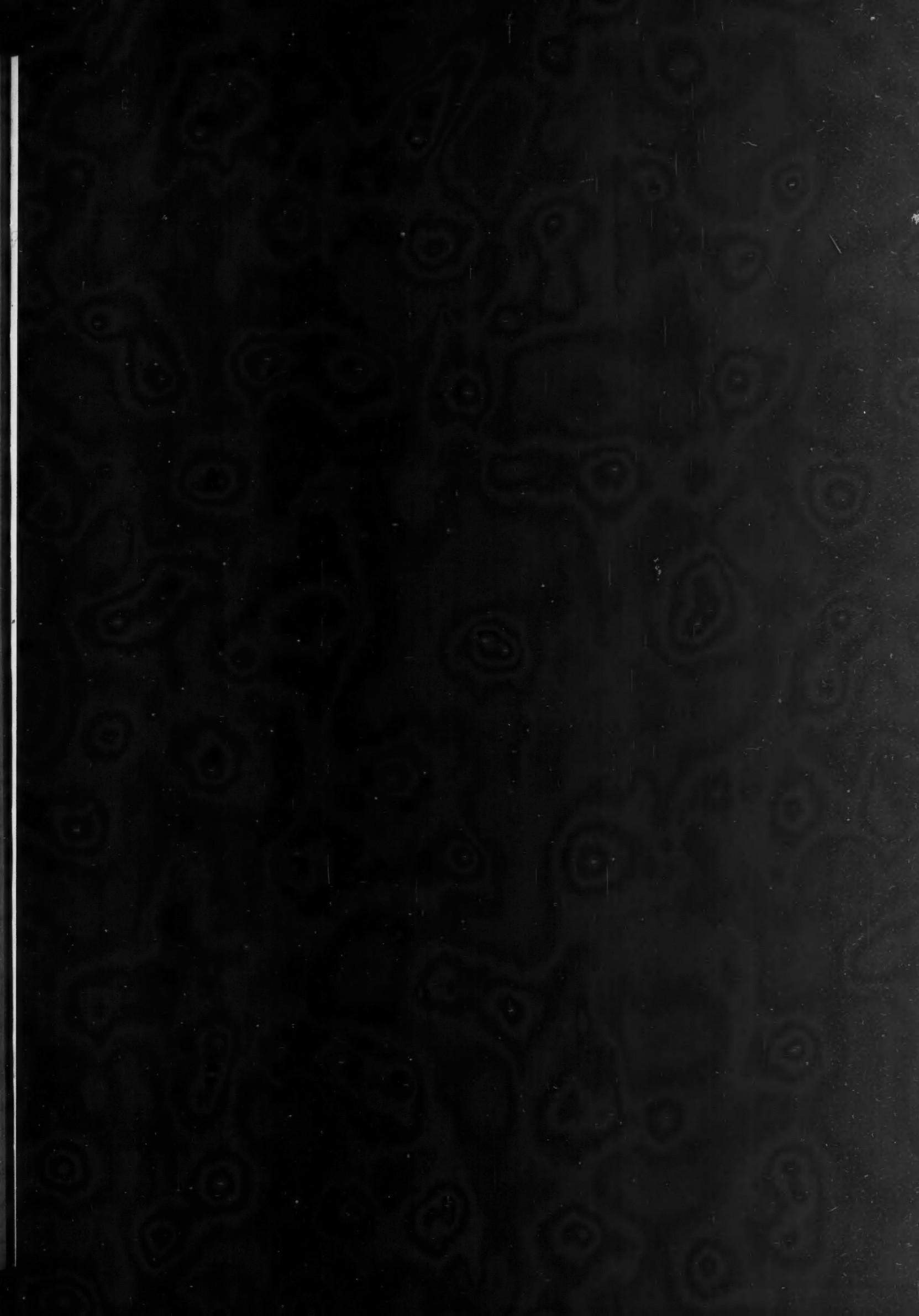
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## MALIGNANT NEPHROSCLEROSIS (MALIGNANT HYPERTENSION)\*

(WITH THE REPORT OF TWO CASES)

BY LEYLAND J. ADAMS, M.D., C.M.,

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IN 1872 Gull and Sutton<sup>1</sup> condemned the narrow view which regarded kidney lesions as the primary factor in all cases of chronic Bright's disease. They referred to a constitutional form of this disease which they called "arterio-capillary fibrosis". They emphasized that in this condition there was present thickening of the arterioles (and, erroneously, of the capillaries) throughout the body, and that the kidneys merely shared in this generalized process. With the introduction of the sphygmomanometer into clinical medicine in 1893 by von Basch<sup>2</sup> recognition of a condition now termed "essential hypertension" was inevitable. Since the classical writings of Sir Clifford Allbutt<sup>3</sup> most clinicians have appreciated the fact that there are various degrees of severity in cases of arterial hypertension. By 1914 Volhard and Fahr<sup>4</sup> divided cases of hypertension into two groups, and designated them as "benign and malignant nephrosclerosis". Later Fahr<sup>5</sup>, as a result of his pathological studies, suggested that the term "malignant nephrosclerosis" be applied only to those cases in which arteriolar necrosis and endarteritis were present in addition to the arteriolarsclerosis present in nearly all instances of essential hypertension. In 1924 Keith and Wagener<sup>6</sup> made a study of a selected group of patients with hypertension, in which

they felt that the clinical findings were sufficiently characteristic to establish the diagnosis of malignant hypertension. The predominant features in the majority of their cases were the sustained high blood-pressure combined with neuro-retinitis, the short duration of the symptoms, the tendency to affect comparatively young people, and the maintenance of good renal function until a late stage. They specially stressed the diagnostic importance of changes in the retinal vessels early in the disease.

We now know that in malignant nephrosclerosis one of most important and outstanding pathological changes occurs in the arterioles. These changes, while pronounced in the kidneys, occur widely scattered throughout the body—in the heart, brain, pancreas, capsule of the adrenal, gastro-intestinal tract, spleen, and skeletal muscles. They have been emphasized by all recent investigators.<sup>7 to 10</sup>

While the majority of cases of so-called "essential hypertension" can be put into one large group, there are undoubtedly cases that do not fit. The term "malignant hypertension" has crept into the literature to describe this small group. There still exists much difference of opinion concerning its fundamental nature. Most authors regard it as a phase or complication of the benign essential (vascular) hypertension (Fishberg,<sup>11</sup> Christian,<sup>12</sup> O'Hare,<sup>13</sup> Rolleston<sup>14</sup> and others). On the other hand, Fahr<sup>7</sup> and, more recently, McMahon,<sup>10</sup> consider malignant hypertension to be a separate and distinct clinical and pathological entity.

\* From the Medical Services of Dr. A. H. Gordon, and of the late Dr. C. P. Howard, and the Pathological Department of the Montreal General Hospital.

This paper is reported in part in "Medical Papers Dedicated to Dr. Henry A. Christian, Feb., 1936."

The occurrence of malignant hypertension must still be regarded as a comparatively rare condition. As a result of an increasing interest in it and knowledge of the pathological changes which characterize it we feel that in the future it will more frequently be recognized clinically. This belief is strengthened by the conviction that a more careful investigation of these cases will make it possible to distinguish malignant hypertension from benign hypertension on the one hand, and from chronic glomerulo-nephritis on the other. We have had the opportunity of studying two cases which illustrate this contention.

#### CASE 1

(M.G.H. No. 6610-33), a Canadian housewife, aged 42 years, was admitted to the Montreal General Hospital, into the service of Dr. A. H. Gordon, on November 7, 1933, complaining of precordial pain and shortness of breath of five years' duration, and loss of weight of six months' duration.

*Family history.*—Her mother died at the age of 54 years, from "sudden heart failure".

*Past history.*—Appendectomy was performed at the age of twenty-one. Her only pregnancy terminated in a miscarriage at seven months. Otherwise the patient had always enjoyed excellent health and lead a very active, even strenuous life.

*Present illness.*—She was perfectly well until five years prior to admission, when she had attacks of bronchitis, and, after coughing, severe precordial pain which was referred to the left side of the neck and down the left arm. Associated with this pain there were marked shortness of breath and a sensation of suffocation. Ever since that time she had had repeated attacks of pain and shortness of breath, especially after exertion. Walking up steps, cooking or doing housework would often precipitate an attack. During the past three years these attacks had increased in frequency and intensity. Even the slightest exertion would bring one on. For a year before entry she was unable to do any work, and attacks occurred while at rest. Weakness became marked, and she lost thirty to forty pounds in weight. Two weeks before admission she became extremely short of breath and noticed swelling of the legs.

*Physical examination* revealed a well developed, well nourished woman, weighing 160 pounds, with obvious respiratory distress but no cyanosis. There was strong visible pulsation of the neck vessels. The pulse was rapid, 120 per minute, regular with good volume and high tension. The blood pressure was 260 systolic, 160 diastolic. The apical heart impulse was diffuse, visible, and palpable in the fourth and fifth interspaces, 15 centimetres from the midsternal line. In addition there was a double thrust at the apex giving a triple rhythm. The heart was greatly enlarged to percussion and by x-ray. There was a loud apical systolic murmur, and at the base both aortic and pulmonary second sounds were accentuated. Numerous râles were heard at the lung bases. The edge of the liver could just be felt. There was moderate pitting oedema of the lower legs. The ocular fundi showed slight bilateral papillœdema, numerous haemorrhages and white spots, as well as marked sclerosis of the arterioles.

The temperature was normal. The pulse averaged 100. The specific gravity of the urine varied from 1012 to 1022; albumin was present in large amounts (three plus); no glycosuria. Microscopically there were 2 to 4 red blood cells and 4 to 6 white blood cells per high

power field, and a moderate number of hyaline casts. The red blood corpuscles numbered 4,800,000; leucocytes 8,700 per c.mm.; haemoglobin 84 per cent (H), and the differential count was normal. The blood and spinal fluid Wassermann tests were negative. The six-foot x-ray plate of the heart showed enlargement of the heart without widening of the aortic shadow. An electrocardiogram showed a left axis deviation with depression of the S-T interval in leads one and two. Blood urea nitrogen was 22, creatinine 1.96, and blood sugar 153 mg. per cent. The basal metabolism was plus 22.

*Clinical course.*—The systolic blood pressure fluctuated between 220 and 270, the diastolic between 120 and 160 mm. of mercury. The oedema of the ankles and the râles at the lung bases disappeared within a few days. Dyspnoea and precordial pain were the main complaints. Twelve days after admission a renal test meal showed a maximum variation of specific gravity of eight points, with no increase in the night volume. Headache, loss of appetite and nausea later became prominent symptoms. Three weeks after admission she suddenly complained of blurred vision and intense severe headache. Fresh retinal haemorrhages and increased papillœdema were noted. A lumbar puncture revealed increased cerebrospinal pressure (500 mm. of water). A phlebotomy of 500 c.c. gave some relief, but 2 days later, she became dull and drowsy mentally. A pericardial friction rub became audible and the blood urea nitrogen had risen to 56 mg. per cent. From this time on the patient failed rapidly. The friction rub persisted; the breath became foul; the blood urea nitrogen mounted steadily to 158 mg. per cent, with the creatinine 8.10 mg. per cent. (See Chart). The respirations became Cheyne-Stokes in type. She developed convulsions and died in uræmia on December 18th, forty-eight days after admission.

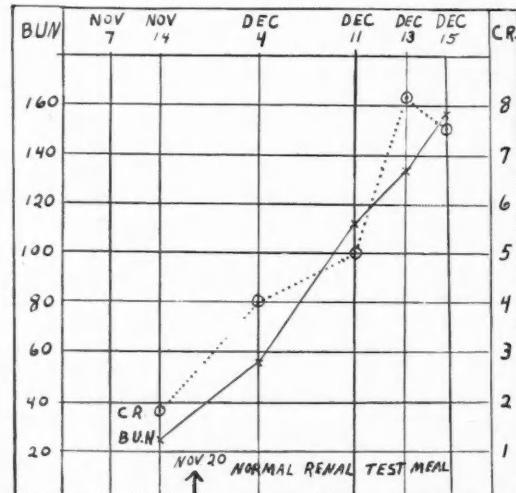


Chart showing the rapid rise in blood urea nitrogen, and creatinine.

*Abstract of post-mortem record* (M.G.H. A-33-256). The heart was markedly enlarged, weighing 600 grams. This was due chiefly to a concentric hypertrophy of the left ventricle, the wall of which was 2 cm. thick, while that of the right ventricle was 0.5 cm. The visceral pericardium was covered with a moderate amount of shaggy yellowish, dense, fibrous exudate. The valves appeared normal and the coronary arteries were patent.

The kidneys appeared of normal size, or even slightly larger; each weighing 165 g. The capsule was stripped with some difficulty, exposing a finely granular, deep red surface. On gross section the differentiation was good, and there were well preserved cortical striations. The cortex measured 0.5 cm. in thickness. There were no petechial haemorrhages.

The aorta was free from any evidence of atherosclerosis, as were also the iliac, renal, splenic and cervical arteries. The lungs, liver, spleen, gastro-intestinal tract showed moderate congestion, but were otherwise not remarkable. The brain was not obtained.

On microscopic examination the blood vessels of the pericardium showed marked congestion, and there was a zone of fibrin deposit upon its outer surface. The muscle fibres were greatly increased in size. Scattered throughout the myocardium were several large and small haemorrhages, areas of myocardial atrophy, and a few foci of round-cell infiltration. One large coronary artery showed early atheromatous changes, and one smaller artery showed hyperplastic thickening of the intima. The following description is a composite picture of the lesions in the kidneys. It is based upon the examination of a series of sections taken from blocks removed from various locations and stained with haematoxylin and eosine, Masson's trichrome, Mallory's phosphotungstic acid haematoxylin, Weigert's elastic tissue stain, azan carmine, scarlet R, and stains for amyloid.

"The capsule is smooth. The glomeruli show a variety of pathological changes. A good many are atrophic, some showing partial and others complete hyalinization of their tufts (Fig. 1); while still others appear normal. An occasional glomerulus appears swollen, stains poorly, and shows red blood cells in Bowman's space. A few better preserved glomeruli also show red blood cells in Bowman's space. The azan carmine stain demonstrates a marked thickening of the basement membrane of many of the glomerular

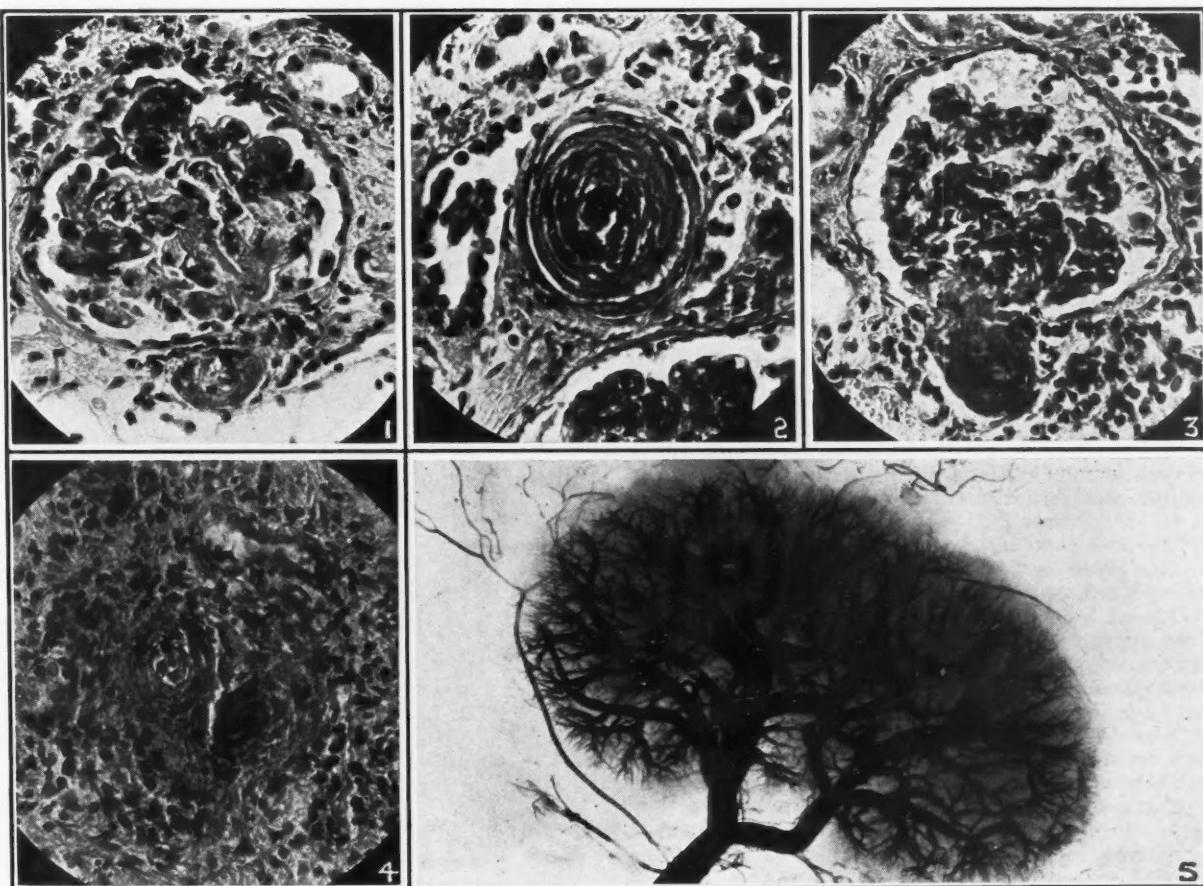
vessels. The larger arteries show comparatively little change; those of medium size show hyperplasia of the walls and reduplication of the internal elastic membranes. The smallest arteries, and especially the arterioles, show a very marked thickening of their walls with resulting narrowing of their lumina (Fig. 2). This becomes a very striking feature in the sections stained with scarlet R. The lesion is especially marked in the afferent arterioles (Fig. 3). There are quite numerous small, irregularly distributed areas of focal necrosis and cellular infiltration somewhat resembling an inflammatory process. These areas are similar to those described by Fahr (Fig. 4).

"In some areas the tubules are dilated, in others they are atrophic and show an increase in connective tissue about them. These two changes are not, however, a striking feature. Scarlet R stains demonstrate marked fatty degeneration of the tubules.

"Lesions of the arterioles similar to those in the kidneys are seen in the spleen, pancreas, peri-adrenal tissues, and in one vessel of the lung."

The pathological diagnosis was as follows: malignant nephrosclerosis; hypertrophy of the heart; exudative pericarditis; congestion and oedema of the lungs (terminal); congestion of the abdominal viscera (terminal).

At the post-mortem one of the kidneys was removed with the renal artery intact, and injected with 20 per cent bismuth oxychloride in 10 per cent gum acacia, according to the method described by Hill.<sup>15</sup> X-ray showed the so-called "barren fig-tree" appearance (Fig. 5).



**Fig. 1.**—Glomerulus showing thickening of the tuft arterioles. Areas of vascular hyalinization.  
**Fig. 2.**—Arteriole showing marked thickening of the wall with narrowing of the lumen. **Fig. 3.**—Glomerulus showing atrophy, albuminous material in Bowman's space, and very extensive lesion of the afferent arteriole. **Fig. 4.**—Focal area in the kidney substance showing acute necrosis and cellular infiltration. **Fig. 5.**—X-ray of kidney, after its injection with bismuth oxychloride. Note the so-called "Barren Fig-tree" appearance, and abundant peri-renal arterial branches.

## CASE 2

(M.G.H. No. 1166-36).—A Canadian housewife, aged 51 years, was referred to the Montreal General Hospital, by Dr. Alan B. Hall, on February 28, 1936, complaining of vomiting, dimness of vision and dyspnoea of only one month's duration.

*Family history.*—Irrelevant.

*Personal history.*—Apart from measles as a child, the patient always enjoyed good health. Married at thirty-four, two children alive and well, two miscarriages.

*Present illness.*—She was perfectly well until four years prior to admission, when at the age of 47 years she stopped menstruating and began to suffer from "barking noises" in the ears. At this time she was told that her blood pressure was high, over 200 systolic. One year before admission, she noticed that she became fatigued more easily and was unable to do her ordinary housework. One month before entry, she began to feel nauseated and at various times vomited repeatedly. About this time she became extremely restless and for the first time noted dimness of vision. One week before entry she consulted an ophthalmologist who told her that she had white patches and haemorrhages in the retinae. From this time on her condition rapidly became worse. Her physician reported the blood pressure to be 238/120, the respirations to be Cheyne-Stokes in type, and urine "that boiled solid".

*Physical examination* revealed a middle-aged female, distinctly drowsy, lapsing into periods of semi-unconsciousness. There was marked pallor, and the respirations were Cheyne-Stokes in character. The pulse was regular, rate 104 per minute, with good volume and high tension. Blood pressure was 230 systolic, 110 diastolic. The apical heart impulse could not be located, but the heart was enlarged to percussion and by x-ray. The heart sounds were clear, and the aortic second sound was accentuated. Numerous moist râles were audible at the lung bases. The liver edge could be palpated one finger's breadth below the costal margin. The right kidney was palpable. There was no œdema of the extremities. The ocular fundi showed marked œdema of the disks, retinal haemorrhages, "white spots" and marked sclerosis of the arterioles.

*Clinical notes.*—The temperature ranged from 98.6 to 100 degrees Fahrenheit, and the pulse varied from 96 to 124 per minute. The urine showed a specific gravity of 1008, and albumin was present in large quantities (four plus). Microscopically, there were 2 to 5 red blood cells and 5 to 6 white blood cells per high power field, and numerous hyaline and granular casts. The red blood corpuscles numbered 2,800,000; leucocytes 13,000 per c.m.m.; haemoglobin 35 per cent, and the differential count was normal. The blood Wassermann reaction was negative. X-ray showed enlargement of the heart. The arch of the aorta appeared normal in size. An electrocardiogram showed changes in the T-wave in leads I and II. Blood urea nitrogen was 73, creatinine 5.45, and the blood sugar 126 mg. per cent.

*Clinical course.*—The systolic blood pressure remained approximately 230, and the diastolic 110 mm. of mercury. Drowsiness, vomiting, restlessness, dyspnoea, and Cheyne-Stokes respirations were predominant features. Within two days, the blood urea nitrogen rose to 115, and the creatinine to 8.10 mg. per cent. The breath became foul. She developed muscular twitchings and died in uræmia March 5th, seven days after admission.

*Abstract of post-mortem record* (M.G.H. A-36-44).—The heart weighed 350 grams. There were no valvular lesions. The aorta showed simple arteriosclerosis. The left kidney, weighing 140 grams, showed a slightly granular surface throughout which were scattered numerous pin-point haemorrhagic areas. On section the cortex and medulla were poorly differentiated, and showed numerous pin-point haemorrhages. The right kidney, which was similar in size and character, was removed with the blood vessels intact, injected with 10 per cent bismuth oxychloride and x-rayed. The roentgenogram

showed almost complete absence of filling of the arterioles at the periphery, in contrast to the large arteries which were well injected. The remaining organs showed no gross lesion. On microscopic examination, the kidneys showed focal areas of haemorrhage, almost universal hyaline changes in the tuft arterioles and the afferent vessels of many of the glomeruli. The medium-sized arteries showed a hyperplastic sclerosis. A striking feature was necrosis of the walls of the arterioles and the vessels within the glomeruli as well as focal areas of necrosis within the kidney parenchyma. Hyaline changes in the arterioles of the spleen and pancreas were present. The pathological diagnosis was as follows: (a) malignant nephrosclerosis; (b) hypertrophy of the heart; (c) atheroma of the aorta.

## COMMENT

While the vast majority (over 90 per cent) of patients with essential hypertension never develop renal insufficiency, the two cases here reported serve to emphasize the fact that it may occur. The first patient showed extreme hypertension, pronounced cardiac symptoms, marked retinal changes and adequate renal function; and while under observation in the hospital developed signs and symptoms of rapidly progressing renal failure, resulting in uræmia and death. The second case is in many ways very similar to the first, in that it showed extreme hypertension, marked retinal changes, and rapidly progressing renal failure, resulting in uræmia and death. Post-mortem examination in each of these cases showed the pathological findings which we consider to be those that characterize malignant nephrosclerosis.

Changes in the eyegrounds were marked in both cases at the time they were admitted into the hospital. Patient No. 2 illustrates the clinical importance of these early changes, in that she consulted her oculist because of sudden onset of failure of vision. It also stresses the necessity that all clinicians be able to recognize gross changes in the fundi. Volhard<sup>16</sup> states "The eyegrounds frequently reveal the first sign of the fatal turn in the form of contracted arteries and the classical picture of retinitis angiospastica". Just why the clinical course of certain cases of essential hypertension should suddenly change to the malignant form has never been fully understood. Volhard adheres to the theory of circulating pressor substances in the blood. Two factors however are of importance in their bearing upon the possibility of the occurrence of this sudden change. They are, the age of the patient, and the height of the diastolic pressure. The younger the individual in whom a genuine hypertension has developed, and the higher his

diastolic blood pressure, the greater is the danger that the disease may take on a malignant course.

The prognosis in malignant hypertension is grave, and at the present stage of our knowledge the treatment must necessarily be symptomatic and palliative in character.

#### SUMMARY

Two cases are reported with characteristic clinical and pathological findings of malignant nephrosclerosis (malignant hypertension).

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#### A CASE OF ALZHEIMER'S DISEASE WITH NEUROPATHOLOGICAL FINDINGS\*

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THE case which I have to present is one of Alzheimer's disease, or early senility. The condition has been studied fairly extensively, but there are certain features, both clinical and pathological, which give rise to difficulty in distinguishing it from true senility. A great deal more study will be necessary before these two conditions, which I believe to be distinctive entities, can be definitely separated. The difficulty is accentuated because there are, at first sight, certain features in the microscopic findings which are common to both, but which, on closer observation, it seems to me, do show definite differences. Clinically, the conditions can be separated by an arbitrary age limit, but such a basis does not remove the conflict which arises when the pathologist is called in. It is with the view of trying to clear up some of these difficulties that the following case is presented.

#### CASE HISTORY

The patient, a female, aged 53, was admitted to hospital on August 16, 1932, with the complaints of gradually developing dementia, loss of memory, periods

of restlessness, alternating with periods of depression and occasional extreme excitability.

*Family history.*—No mental or nervous disease in the family nor alcoholism or drug addiction were reported in any of the members.

*Personal history.*—As a child, the patient was bright in school, completing her high school education. She was always adjusted socially, becoming a leader in church activities and singing in the choir. She was capable of playing several musical instruments. After graduation from high school she lived at home with her mother and sister. She was very much attached to her sister, to the extent that she wished to live with her even after the sister's marriage. Although a good mixer with the female sex, she never had anything to do with the male, and there was a tendency toward a homosexual attitude.

*Medical history.*—There was nothing of note in the medical history. Alcoholism, drug addiction, venereal disease, and sexual relationship were denied. There was no record of previous nervous or mental disease prior to the onset of the present illness.

*Personality.*—The patient was reported to have been an extroverted type, jolly, clever and a good worker.

*Onset of the present illness.*—Following the death of the patient's mother, twelve years before admission, it was noted that the patient became preoccupied, on some occasions did not appear to hear conversation directed towards her, and frequently forgot matters in which she had been very punctilious. She became less careful about her house work, and occasionally would laugh foolishly. She brooded considerably over her mother's death, frequently refusing food and drink. There was a report that up to four years previous to admission, she had occasional spells when she appeared to lose consciousness, during which time she remained rigid, to such an extent that a strong person could not open her hands. She did not become blue and did not cry out, nor did she have any incontinence during these attacks, and recovered rapidly. During the four years previous to admission, these spells were not noted, but she became more forgetful, preoccupied and childish in her actions.

\* From the Neuropathological Laboratory, Ontario Department of Health and Division of Neuropathology, University of Toronto.

Read before the Section of Nervous and Mental Diseases, American and Canadian Medical Associations, Atlantic City, June 12, 1935.

She was, however, quite manageable and helped with the housework in a moderately satisfactory manner until August 5, 1932, ten days previous to admission, when she suddenly became excited for no apparent reason. She would run about the house in complete confusion, mumbling in an unintelligible manner, and laughing hysterically at times; would scream at the top of her voice for several minutes. She became abusive to her sister and brother-in-law with whom she was living, and destructive to her own clothing and articles about the house. On one occasion, she upset the dining room table with all the dishes on it. These periods would abate to some extent, but would recur, and during them she would strike anyone who came near her. She had no idea where she was or what she was doing. She was deported from the States to Fergus, Ont., where she was certified by Drs. A. Groves and F. T. Russel. She was admitted on August 16, 1932. The certificates recapitulate the foregoing history, and added that the patient had for some few days to be cared for like an infant and could not feed herself.

*Mental examination.*—When first admitted, the patient was deeply under the effects of sedatives. Shortly after admission, when the effects of the sedatives had worn off, she became restless, running about the ward and refusing to stay in bed. She was given appropriate clothing and allowed to be up. Mental examination was quite impossible due to the lack of intelligence, inability to speak, and excitability. Her conversation consisted of mumblings, and she responded with a foolish grin to questions, and occasionally by some little impulsive act such as grabbing the examiner's pen or his necktie. She offered physical resistance to being put to bed, and was content only to wander about here and there, keeping up the while a stream of mumblings interspersed with periods of foolish laughter. Following her admission, she showed no extreme excitability and there was no evidence of violence so long as she was allowed to wander about. It was impossible to state whether hallucinations or delusions were present or to estimate the power of her memory. It was the examiner's opinion that she was completely disoriented and did not know what she was doing. The examination was abandoned at this time. Further examination on November 15, 1932, gave the following impressions and information. "When one tries to enter into conversation with this patient, the most outstanding feature is the degree of dementia which is present and is very profound. It would appear as though she had no appreciation whatsoever as to what is going on, or what is being said to her. Any attempt to test her aphasia is fruitless."

The wandering was still present. She was unable to find her way back to her bed, and was apparently unconscious as to whether or not she had any clothing on, and she had to be dressed and fed. She was unclean in her habits. The expression was a fixed smile and never varied, and there was continued mumbling which was quite unintelligible. There was a slight suggestion of carrying out commands when asked to close her eyes or put out her tongue. When asked her name she gave it correctly and then continued to repeat it four or five times. When asked when she came to hospital she repeated the last word half a dozen times. This tendency to repetition was on some occasions quite marked. At this time the differential diagnosis was thought to lie between general paresis, frontal lobe tumour, arteriosclerosis, dementia praecox, senile psychosis.

It was thought, on account of the long history and absence of localizing signs that brain tumour was unlikely. The age and mental picture were thought to exclude dementia praecox. The blood Wassermann test and spinal fluid reaction were negative; there was no history of luetic infection and it was therefore ruled out. The degree of arteriosclerosis on physical examination was not extensive, and this was ruled out. The examiner states: "The diagnosis seems to rest with the early senile group, and the case is being considered as one of Alzheimer's disease".

*Physical examination.*—Weight on admission, 83 pounds. The patient looked thin and ten years older than her stated age of 53 years. Due to lack of co-operation, the examination was very unsatisfactory. It was noted, however, from fleeting glimpses of the eye grounds, that they were pale but sharply defined, and it was thought that a moderate degree of arteriosclerosis was present. Nothing significant was noted about the head and neck or the chest. In the cardiovascular system, numerous extra systoles were noted; the left border of the heart extended 9 cm. left of the mid line in the 5th interspace and 3 cm. to the right in the 4th interspace; there was a slight mitral systolic murmur. The peripheral arteries were slightly palpable. The abdomen was negative. No vaginal or rectal examination was done, because of lack of cooperation.

*Cranial nerves.*—The first and second could not be tested; 3rd and 4th and 6th, pupils reacted to light and accommodation; the eye movements were apparently normal, but the examination was unsatisfactory. The 5th and 7th nerves appeared normal; the 8th could not be tested, but from the various partial response to commands it appeared she could hear. The 9th and 10th were negative, as was the 12th.

*Reflexes.*—The biceps, triceps, patellar and ankle jerks were equal, but slightly hyperactive. The plantar reflex was normal and there was no clonus. Coordination could not be tested. Speech could not be satisfactorily tested, but the patient sometimes repeats simple words such as King, King, King, or Peggy, Peggy, Peggy, but this is the extent of the conversation.

*Sensation.*—No cooperation could be obtained, but she apparently felt pin prick throughout.

*Gait.*—The patient was weak, walked in a halting fashion, which it was thought could be accounted for by the degree of emaciation present.

At a conference of the staff on October 3, 1932, the case was diagnosed as Alzheimer's disease. On November 16, 1932, the patient was presented as a case of Alzheimer's disease at an inter-hospital conference. Considerable discussion was provoked after the diagnosis, but no other conclusion was reached.

*Progress notes.*—On December 22, 1932, the nurse in charge of this case noted a seizure which was tonic in type. The eyes were fixed, staring upwards, and the patient was frothing at the mouth. Some time following the seizure there was incontinence. The patient was receiving sedatives to control restlessness. On January 23, 1933, a further seizure was described by the nurse, occurring early in the morning, with twitching and involuntary contractions of the muscles. At this time there was incontinence during the seizure. In neither case was there any biting of the tongue. She showed some slight sign of drowsiness following the seizure, but it was not felt that the seizure was truly epileptic. On May 10, 1933, a further seizure occurred early in the morning, but with no after-effects. On July 29, 1933, a seizure of 20 minutes' duration was reported early in the morning, when she fell to the floor. Another seizure occurred on that date two hours later, which lasted for one hour, after which the patient was quite drowsy and her pupils reacted rather sluggishly to light. There were no localizing signs and no paralysis, and the seizure was thought probably due to arteriosclerotic spasm. Because of the appearance of the attacks in the early morning a hypoglycaemic epilepsy should have been considered. A similar seizure occurred August 16, 1933, and again on August 21, 1933. A note on January 10, 1934, states: "that the patient had been gradually growing weaker from day to day and died about 1 p.m. with a hypostatic pneumonia".

*Laboratory findings.*—The blood and cerebrospinal fluid gave a negative Wassermann test.

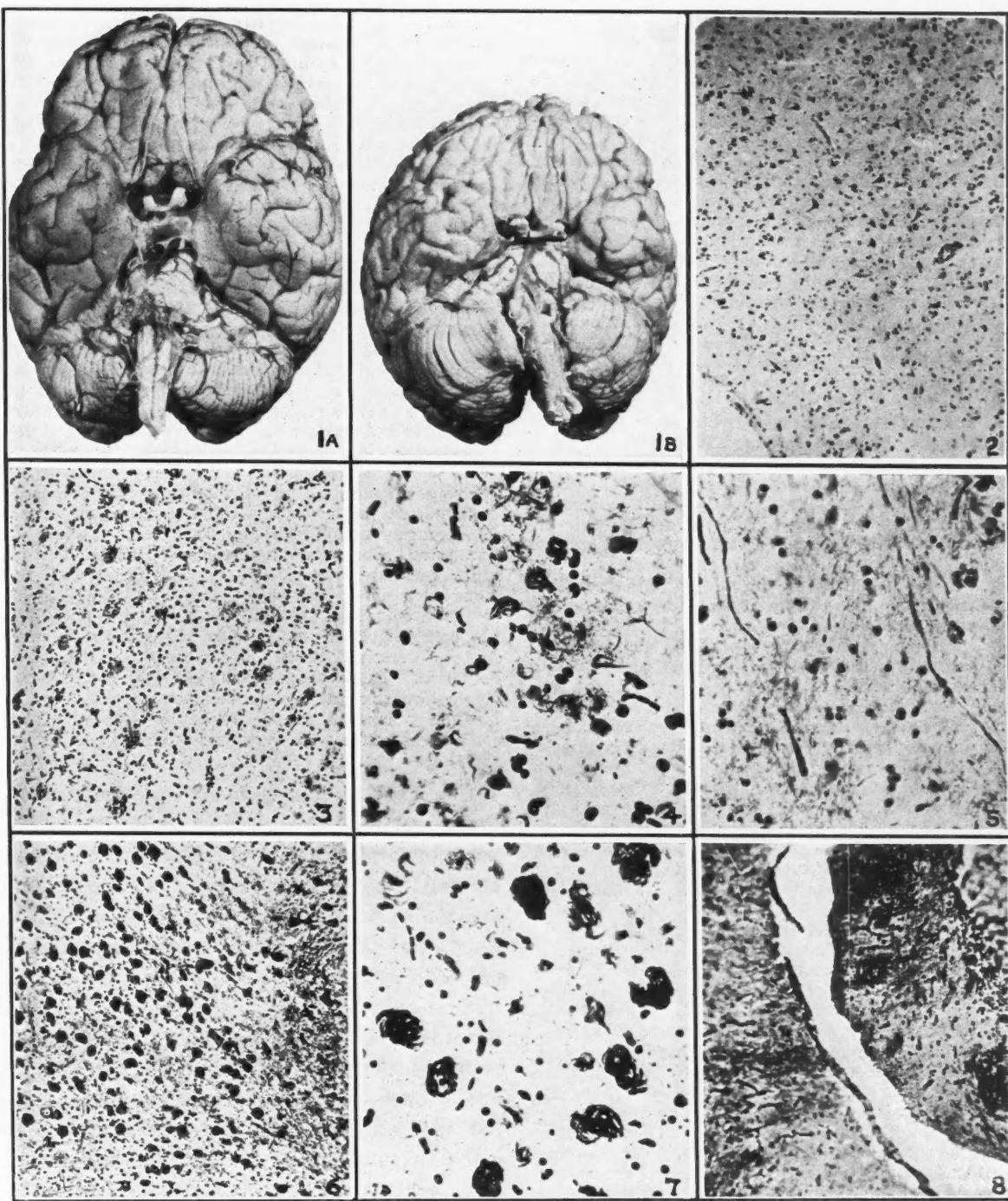
*Autopsy.*—This was performed on the date of death. The body showed extreme emaciation and looked ten years older than the stated age.

Hypostatic pneumonia in the lungs and some degree of sclerosis in the coronary arteries, and chronic sclerotic

endocarditis of both the tricuspid and mitral valves were found.

**Brain.**—The brain weighed (after fixation) 825 grams. The dura was markedly adherent to the skull cap and there was some increase of cerebrospinal fluid in the subarachnoid space. The brain itself was small, and the sulci were widened and deepened.

**Examination after fixation.**—There was extreme atrophy of the gyri throughout, but most marked in the frontal poles. The vessels at the base showed a few atheromatous plaques, but were, generally speaking, fairly well preserved. There was some thickening of the arachnoid around the base. The whole structure appeared small. The hemispheres were separated by in-



**Fig. 1A.**—Normal brain, weighing 1,230 grams, compared with **Fig. 1B**, brain from a case of Alzheimer's disease, weighing 825 grams. (Slight distortion in fixation in the brain of Alzheimer's.) **Fig. 2.**—Section of the cortex and white matter frontal pole, cresyl violet stain, showing extreme loss of nerve cells and degenerative processes in those remaining. **Fig. 3.**—L.P. Cortex frontal pole, right, Cone and Penfield's silver carbonate method, showing a large number of plaques. **Fig. 4.**—H.P. view of plaques seen in Fig. 3, showing plaques and Alzheimer's tangles. **Fig. 5.**—White matter frontal lobe, Cone and Penfield's silver carbonate method, showing secondary degeneration in neurofibrils. **Fig. 6.**—Nest of nerve cells in globus pallidus, L.P., showing tangles within the nerve cells. Note sharp limitation of the destructive process to the nerve cells. **Fig. 7.**—H.P. view of area from Fig. 6, showing tangles and early plaque formation within the nerve cells. **Fig. 8.**—Cerebellar cortex, Cone and Penfield silver carbonate method, showing plaques.

cision through the corpus callosum and brain stem. The atrophy of the gyri on the mesial surface was as marked as on the vertex. The pineal gland was cystic and calcified. The whole brain had a peculiar gelatinous appearance. The ventricles showed marked internal hydrocephalus. A transverse section was made through the right hemisphere, and showed a thinning of the corpus callosum and loss of white matter and thinning of the cortex. A further section made through the basal nuclei showed them to be shrunken, and there was peculiar streaking of the globus pallidus, which was sharply differentiated from the putamen. There was some streaking of the caudate nucleus as well as the globus pallidus, and the nuclei cut with considerable increased resistance to the knife.

Although the atrophy of the gyri was widespread, there was a marked lack of prominence of the frontal lobes, and the sulci in this region were much wider than in others. The frontal lobes were not only foreshortened, but were much thinner in a vertical direction than the normal brain. The whole structure, as indicated by the weight, was markedly reduced in size (see Fig. 1).

*Microscopic findings.*—Section of the vertebral artery, right side, showed a considerable amount of endarteritis, the lumen being reduced to half its normal size. The medial coat showed no marked changes, but there was a considerable round cell infiltration of the adventitia. The internal elastic lamina was seen to be intact, and presented the usual wrinkled appearance underneath the thickened intima. This thickening was not apparent to the naked eye in the other basilar vessels.

A section from the left frontal pole, stained with haematoxylin and eosin, showed some degree of thickening of the arachnoid with a slight amount of round-cell infiltration. The vessels of the meninges were somewhat engorged and at one point in the section examined there was a considerable collection of free blood in the arachnoid tissues. The cortex showed a mild increase in the surface glial tissue, the arterioles were somewhat engorged, and, very occasionally, some degree of thickening of the arteriolar wall was noted. The nerve cells were extremely rare throughout the cortex and those remaining were very degenerate in appearance. There was a relative increase in the number of interstitial nuclei noted. The white matter showed a marked increase in the number of interstitial nuclei present. Cresyl violet showed the cortex to be very thin and nerve cells are extremely scarce. Some fields showed a total absence of such cells; those which remained were pyknotic and hypochromic in appearance, some were granular and not a normal nerve cell was seen in the section examined (see Fig. 2).

Examination of a section from the right frontal pole by the Cone and Penfield silver carbonate method showed a tremendous number of the so-called plaques (see Fig. 3). A number of compound granular corpuscles were seen throughout the cortex, and the neurofibrils were broken up and granular, and there were skein-like and basket-like forms. Under high power some of the senile plaques were seen to contain what appears to be degenerating forms of neurofibrils (see Fig. 4). Most of the plaques were seen to contain globular masses which have the appearance of cell nuclei. The remainder of the plaque was formed of granular debris. Occasionally, structures which had the appearance of degenerating fibrils could be seen lying within the plaques. The plaques were not surrounded by any process of gliosis which we could discern. There was no evidence of increase in the number of astrocytes or of glial fibres. Some of the plaques showed some degree of concentric arrangement of the granules. Some formations were noted which had the appearance of nerve cells, with granular masses which apparently represented degeneration of the intracellular neurofibrils. Only a very few normal neurofibrils were noted in any parts of the section examined.

A block from the white matter of the central portion of the right frontal pole was impregnated by the Cone and Penfield silver carbonate method, and many of the

neurofibrils were seen to be swollen, granular and irregular in outline. Nothing resembling the appearance of the senile plaques as found in the cortex was noted anywhere in this section (see Fig. 5).

A section from the basilar nuclei showed a large number of corpora amylacea in the subependymal region and region of the internal capsule. Cresyl violet stain of the basal nuclei showed the nerve cells to be in a degenerating state, slightly less advanced than it appeared in the cortex. A block from the same region, treated by the Cone and Penfield silver carbonate method, showed definite changes within the nerve cells in the putamen and globus pallidus. These are well demonstrated in Fig. 6. They also offer a suggestion that the plaques originate in nerve cells, since they were completely surrounded by white matter, and the tangles and beginning plaques definitely were confined to the nest of nerve cells shown. Under the high power, these masses were seen to be composed of tangled skeins of neurofibrils (see Fig. 7).

A section taken from Broca's area, treated by the Cone and Penfield silver carbonate method, showed a tremendous number of senile plaques, some of which contained remnants of degenerating fibrils. Sections from this region stained with haematoxylin and eosin showed no structures which could be definitely called nerve cells. There was considerable engorgement in the capillaries in this region. These changes were noted in a more or less marked degree in the following additional regions: the upper end of the precentral gyrus right side; occipital pole, left side; region of Ammon's horn left side; insula on the right side. In addition, the thalamus on the left side showed a number of cells with degenerating neurofibrils and, in various regions, skein-formation. Some regions also showed an increase in the number of astrocytes. None of the typical plaque formations were noted, but some areas were very suggestive.

The cortex of the cerebellum showed quite definite plaque formations. In addition, there was some increase in the interstitial tissue; and rod-cell formations could be noted. These plaques were entirely confined to the cortical matter in the cerebellum (see Fig. 8). The medulla oblongata in the region of the olive showed some areas which were very suggestive of plaque formations.

*Comment on the pathological findings.*—The diffuse atrophy showed the process to have been very generalized. It would appear that this atrophy was most marked in the frontal lobes, although distortion in fixation makes it difficult to be sure. Microscopically, Broca's area showed the largest number of plaques, with the frontal lobes a close second. Clinically, mental deterioration and aphasia were early and severe manifestations. The involvement of the basal nuclei in more recent formations might suggest that the agitation and unsteadiness might have had part, at least, of their origin in lesions in this locality. The sleeplessness and loss of weight might also be linked to disturbances of vegetative functions of this area. The thalamus showed sufficient change to account for the emotional instability. From a general point of view gliosis was not a predominant feature, although localized areas were found. The wide distribution of plaques throughout the nerve cell-containing areas, and their absence in the

white matter is very suggestive of their relationship. Arteriosclerotic changes, although present in both the larger arteries and the arterioles, were no more marked than we have seen in cases showing absolutely no mental manifestations, and cannot be said to have played any very significant rôle.

#### DISCUSSION

Alzheimer's disease was first described by that author<sup>1</sup> in 1907. Up to the present time over 90 cases have been well described in the literature. Krapf<sup>2</sup> has given the most extensive bibliography, and those writers of more recent date, not mentioned by Krapf, have been noted by Rothschild.<sup>3</sup> Numerous doubtful cases have been reported. Alzheimer's original description contains cases in the sixth decade. Perusini<sup>4</sup> gave a comprehensive discourse on the disease, but he also confused it with true senility, some of his cases being in the sixth decade also. Barrett<sup>5</sup> gave a description of 8 cases, but included some with histories starting in the seventh decade. The inclusion of cases beginning after the fifth decade of life, we feel, confuses the issue. In all probability such cases are of true senile origin, rather than the Alzheimer's reaction.

There are, however, many points of similarity between the two types, loss of memory, general dulling, memory retention disturbances, impairment of judgment, lack of initiative as compared with the individual's normal self, lack of interest in, and ability to concentrate on, matters formerly of interest, and disturbances of the affect tone, are characteristic of both conditions.

There are, however, certain clinical features which ear-mark the Alzheimer's or early type of senility. Grunthal has conveniently divided the condition into three phases.—

1. A stage of gradual loss of memory and disturbances in perception, carelessness in work and appearance, disorientation for place, weakness or epileptiform attacks, with some loss of words and slurred speech.

2. Complete disorientation for time, place, and person, dulling of comprehension, inability to read, write or do sums in simple arithmetic.

3. A stage of extreme irritability with paraphasia, uncleanliness, and stereotyped movements.

The case we have reported showed all these stages. Most marked were the speech disturbances, rapid mental deterioration, and agita-

tion. The early appearance of such conditions aids considerably in arriving at a conclusion. It would seem that the "youthful senile" suffers from a loss of control over a dynamic organism, while the senile shows a deterioration of the whole organism, and pursues his downward course with an accentuation of his former personality. In the first case one system is disorganized; in the second there is slowing and degeneration of the whole anatomical structure. True, the two may overlap in symptomatology, but the one is typical of energy, misdirected, especially in the early stages, while the other is exhaustion of the whole organism from the start.

Recent workers have tended toward a distinction between these groups, both from the clinical and pathological point of view. Lowenberg and Rothschild,<sup>6</sup> as well as other writers,<sup>7, 8, 9</sup> have reported cases with certain basic conditions such as syphilis, and chronic infection, and offer the suggestion that the changes found in the nervous system were secondary to either infection or toxæmia.

MacDonald Critchley *et al.*<sup>10, 11</sup> have attempted to distinguish microscopically, to some extent, between the plaques of Alzheimer's disease and those of true senility. Personally, we have noted that the plaques in cases of early senility and those of true or late senility have quite different appearances, those of the Alzheimer's type being much more widespread, Alzheimer's tangles are more common, and the microglial reaction is absent around the plaques. In late senility the plaques are smaller, fewer in number, and rod-cell formation around the plaque is usual. Within the limits of our experience we feel that no case having an onset after the middle "fifties" should be classified as Alzheimer's disease, unless under very exceptional circumstances. We feel also that a more thorough study of both types of cases, done under separate classifications as to age, is essential before a definite distinction can be made. Our own material is much too limited to warrant more than tentative conclusions. From what material we have seen and from the work of others we suggest that there is a distinct pathological difference between the two types of cases.

As regards the origin of the plaques, two theories have been put forward. First, that they originate from the interstitial tissue, or that they originate in nerve cells and later are added

to by the interstitial tissue. The second theory holds that they originate solely from nerve cells, and that whatever is contributed by the interstitial tissue is merely reaction to destruction of tissue and bears no relationship to the origin or formation of the plaque. In the case we have presented we have stressed the point that the plaques could only be found in those locations where nerve cells were found, and the number of plaques bore a definite direct ratio to the number of nerve cells found in any location. This we have found true, regardless of whether the case was one of early or late senile psychosis. We are therefore of the opinion that plaque formation depends entirely upon the presence of nerve-cell bodies for their formation, and that interstitial reaction is dependent upon destruction of nervous parenchyma.

#### CONCLUSIONS

The case presented offers a unique history of this condition. The onset of symptoms in an otherwise normal person at the age of 41, of gradual mental deterioration with loss of memory; epileptiform seizures, not characteristic of epilepsy; early aphasia, with perservation of gradually increasing severity; periods of excitability, with aimless wanderings and disorientation, all progressing to a profound degree; and eventually unsteadiness with increasing epileptiform seizures, becoming more characteristic of epilepsy, all point to the picture of Alzheimer's disease. The total duration of the disease was twelve years, which is rather longer

than usual. The pathological and microscopic findings confirm the clinical diagnosis, and are, typically, those described in the literature. So far as we have been able to learn, only two other authors have demonstrated plaques in the cerebellum, Barrett<sup>5</sup> in 1911, and Rothschild<sup>3</sup> in 1934. The appearances of the neurones in the olive were very suggestive of early plaque formations in our own case. The remainder of the central nervous system was not available for examination.

In conclusion I wish to offer my thanks to the Ontario Hospital, Hamilton, for supplying the clinical history, and allowing me to present it along with pathological studies. Dr. E. A. Linell offered some very helpful criticisms and suggestions. To Dr. Margaret S. Thompson I am grateful for her careful technical preparations, from which the photomicrographs were produced through the kindness of Dr. D. A. Irwin, Department of Medical Research, University of Toronto.

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**TINNITUS.**—W. J. McNALLY *et al.* present a study of 19 cases of tinnitus, all cases of objective tinnitus being excluded, in patients of widely different ages and with different types of ear disease; most of the patients complained more of the tinnitus than of deafness. The condition may be caused by a lesion in the nerve tissue in Ménière's syndrome by intracranial disease, and possibly by otosclerosis. However, Crowe and others did not find tinnitus a prominent symptom in cases of cochlear disease, and a study of 351 patients showed that tinnitus was present in 10 per cent without obvious local ear disease. The ages of the patients in the present series ranged from 19 to 52 years, and the duration of the condition varied from a few months to thirty years. The younger patients or those who had had tinnitus for a short period did not improve as markedly under the

various treatments as the older ones or those with tinnitus of longer duration. Ephedrine and bellafoline caused improvement in a greater number of cases when given orally than hypodermically. Stimulation of the sympathetic or depression of the parasympathetic nervous system was slightly more beneficial than the converse procedures. Stellate ganglionectomy (depression or elimination of the sympathetic) produced improvement in 3 out of 4 cases. All measures were directed towards altering the cerebral circulation or cerebral pressure; the drugs used produced their full physiological effect, and they have been shown to act on the cerebral vascular mechanism. Despite the undoubtedly alteration of the cerebral circulation, the tinnitus in most cases was unaffected by the measures employed.—*J. Laryngol. & Otol.*, June, 1936, p. 363. Abs. in *Brit. M. J.*

## FILLING DEFECTS IN X-RAY PICTURES OF THE STOMACH DUE TO DISEASE OF ADJOINING STRUCTURES\*

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ABNORMALITIES in pictures of the stomach due to enlargement or inflammation of adjoining structures are of course details with which the expert radiologist is quite familiar, and doubtless he may wonder at a clinician's interest in re-stating or reproducing what to him may seem merely something met with in the course of a day's work. On the other hand, in the two cases which I shall briefly describe neither expert radiologist nor skilled diagnostician seemed able to say very definitely what might be producing the rather unusual pictures which were obtained in repeated exposures. In the one case a distinctly unusual finding is recorded in association with a hypernephroma on the left kidney; in the other, a case of acute pancreatic necrosis, the pressure from fluid accumulating in the lesser sac produced a picture which puzzled all observers, a picture which, though occasionally described, is probably not often seen, since, after all, accumulations in the lesser sac of the peritoneum associated with acute pancreatic disease must very rarely come before the radiologist.

Filling defects of large areas due to extra-ventricular conditions are frequently enough described in connection with enlargement of the spleen, enlargement of the left lobe of the liver, and at times with marked distension of the gall bladder; they have been described in connection with tumours or cysts of the pancreas; and it has long been known that a tumour arising from the upper pole of the kidney or from the adrenal may produce a filling defect if it reaches high enough to press upon the posterior wall of the stomach. It has been occasionally noted that distension of a short, highly-placed transverse colon may produce a filling defect from below, as may, of course, any swelling of large size extending upward from the abdomen.

During the course of an x-ray examination pressure applied from the front produces a characteristic filling defect. It is usually impossible, however, to produce a similar filling defect of the stomach by pressure from behind. Pressure from sub-diaphragmatic accumulations do not seem to produce filling defects in the same ready manner as do tumour growths, and the determination of the presence of fluid under the diaphragm usually helps to explain any questionable finding in the stomach picture. Accumulations of fluid in the lesser sac of the peritoneum might tend to produce the same type of filling defect as do large tumours of the pancreas, and it would seem by no means easy to say whether in certain cases tumour or lesser-sac accumulation is producing the picture before one.

With this brief sketch of extra-ventricular conditions which may produce filling defects in the stomach it may be interesting to consider the radiological reports and the findings in two most interesting cases which have come to our notice in recent months.

### CASE 1

W., aged 40, admitted complaining of weakness, epigastric pains and loss of weight of uncertain origin. It had been noted in the general examination that while lying prone a shadow could be seen to descend from the costo-vertical angle on the left side. This shadow seemed to be produced by the lower pole of the left kidney. There was nothing of a similar nature to be noted on the right side. Palpation in the area of the shadow's descent allowed one to feel a tumour-like mass, thought to be the left kidney, ascending and descending during the act of breathing. This tumour mass was considered to be the left kidney, probably displaced by some structure surmounting it, though in the early weeks of examination nothing suggestive of overlying tumour could be found. A slight deformity of the kidney pelvis could be demonstrated, a deformity suggesting pressure from above, and it could be seen that the kidney was displaced. A catheter passed easily into the left kidney pelvis. A slight enlargement of the spleen was noted, an enlargement, however, not great enough to displace the splenic flexure of the colon.

On carrying through a barium series, it was noted that as the patient lay on his back the stomach outlines were clearly defined and nothing of the nature of a filling defect showed in any screening or picture. On placing the patient prone, however, an enormous filling defect came promptly into view (Figs. 1 and 2). This filling defect needed no external pressure to produce it and remained constant as long as the patient lay upon

\* From the Department of Pensions and National Health, Christie Street Hospital, Toronto, services of Drs. C. E. Cooper Cole and J. D. Mills.

Read before the Section of Medicine, Academy of Medicine, Toronto, on February 11, 1936.

his stomach; it would disappear, on the other hand, the moment he was placed upon his back. The suggestion was therefore made by Dr. Thomas that in view of the evident displacement of the left kidney, as suggested by inspection and palpation and as proved by radiological picture, and in view of the curious filling defect evident in the prone position, some tumour mass, arising from the top of the left kidney, was projecting upwards far enough to fall forward on the posterior wall of the stomach and thus produce the enormous filling defect by its pressure. In no other way, was it felt, could a filling defect behaving in this peculiar way be produced. An exploratory operation some weeks later by Dr. Shenstone revealed that this was the actual state of affairs. A report on the situation of this tumour and its nature has been made by Dr. Lougheed and Dr. Shenstone and will appear elsewhere. Sections showed that the new growth could best be described as a carcinoma of the adrenal. The patient died one year later with symptoms of metastases in the liver and spine.

In the production of Fig. 2, by the simple physical method of placing the patient prone some degree of undue mobility must be ascribed to the tumour springing from the adrenal. Pressure defects of similar form have been fre-

#### CASE 2

G., aged 42, admitted for plastic operation in connection with osteo-periostitis of the right zygoma. Within ten hours of the operation under a general anaesthetic the patient was seized with acute pain in the epigastrum, with vomiting, and with signs of great prostration. His temperature and pulse rate rose, and with these symptoms there was acute tenderness in the epigastrum. There was a very distinct rigidity in the epigastric area for a few hours, which seemed later to be replaced by a deep-seated sense of resistance. The white blood count rose rapidly, and as there had been nothing in the man's history to suggest gastric, duodenal or gall bladder disease the diagnosis of acute pancreatitis was made. The surgical consultant inclined against operative procedure, and during the next ten days a slow, gradual improvement was noted, though there still remained a feeling of deep-seated resistance in the epigastric area, an elevated white blood count, and a temperature reaching 99 to 99.5°. At this time it was considered feasible to put the patient through an x-ray examination of the stomach, though, unfortunately, at the same time he began to show signs of recurring irritation. Careful consideration of symptoms and physical signs inclined us now to believe that one of the accidents associated with pancreatitis, preferably accumulation of fluid in the lesser sac, was producing the symptoms and signs now present in this troubous case, or



Fig. 1



Fig. 2

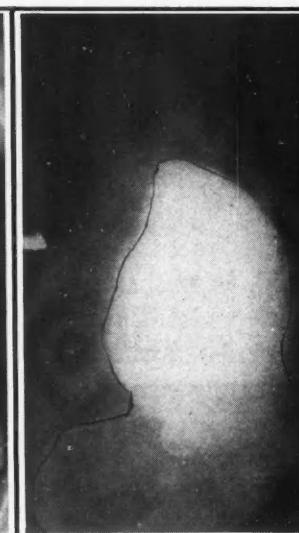


Fig. 3

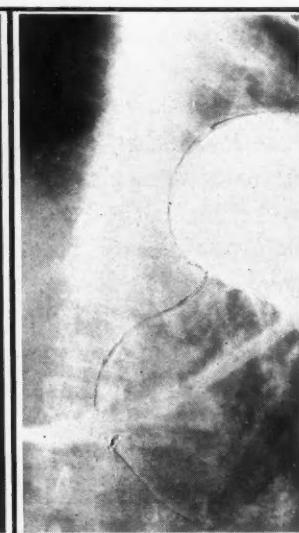


Fig. 4

**Fig. 1.** (Case 1).—Suprarenal tumour; the normal-appearing stomach seen as the patient lies on his back. **Fig. 2.**—The same patient lying on his stomach. Constant filling defect probably due to falling forward of the suprarenal tumour. The filling defect remained constant in all exposures, but disappeared when the patient was placed on his back. **Fig. 3.** (Case 2).—Retention of the barium in the upper two-thirds of the stomach and absence of peristaltic movements. **Fig. 4.**—The same case. Duodenal tube *in situ*. The inability of the stomach to originate peristaltic waves and to push the barium downwards is suggested by the picture. The tube has pushed some barium over the surface of the filling defect.

quently enough described in connection with new growths of the kidney and adrenal, but they seem to have been in most instances pressure defects constant in all positions. One suggests from the report of this case that Dr. Thomas' photographs allow one to infer that a filling defect behaving as does the one we have just described is produced by a freely movable tumour springing from the adrenal or upper pole of the kidney.

that an unsuspected ulcer about the pylorus or in the duodenum was causing symptoms of obstruction by either an acute inflammation of the stomach or bowel wall or by perforating into the lesser sac. The opinion of the many consultants, both in and outside the hospital, and the opinion expressed by the majority of the latter was clearly in favour of the view that the underlying cause of the patient's trouble was a gastric or duodenal ulcer. One notes, in passing, that Dr. Carveth, senior resident of the hospital, adhered throughout to the idea that the man's illness hinged entirely upon a pancreatitis, the origin of which must remain obscure.

With the persistence of symptoms of vomiting and discomfort in the upper abdomen it was felt now that an investigation of conditions about stomach, intestine,

gall bladder and pancreas was demanded, and an exploratory operation was done by Dr. Shenstone. The stomach and duodenum were found free of ulcer, the gall bladder was distended and inflamed. There was some small amount of fluid in the peritoneal cavity, the fat of which was studded with areas of fat necrosis. The whole pancreas was involved in a process of haemorrhagic necrosis, with perforation both into the lesser sac and through the wall of the duodenum, destroying the diverticulum of Vater and allowing fluid to pour out from the lesser sac into the duodenum. This fluid was found in large amounts when the duodenal tube could be made to pass the cardiac end of the stomach. It seemed probable from the nature of the patient's vomitus that pressure from below would force this blood stained fluid past the pylorus and lower part of the stomach, even though the cardiac end of the stomach had seemed unable, judging from the x-ray plates, to push stomach contents downwards. Little could be done to help the patient and he died five weeks after the onset of his acute pancreatitis, a pancreatitis whose complications had seemed to make an accurate diagnosis extremely difficult.

The pictures of the intestinal tract (Figs. 3 and 4), taken when first the man seemed to be improving, show findings which seem extremely difficult to explain. To the eyes of a visiting radiologist they seemed to indicate that no collection of fluid existed in the lesser sac or under the left lobe of the diaphragm. He felt that some inflammatory lesion in the walls of the stomach or duodenum, probably associated with ulcer, was giving the peculiar picture, and to this view a prominent abdominal surgeon inclined, saying that he thought the great dilatation of the stomach must be due to some obstruction in the duodenum resulting from the presence of an old ulcer. The opinion was expressed by a medical consultant that the condition was due to an acute duodenal ulcer, with oedema of the walls of the stomach and duodenum explaining the curious pictures reproduced.

Pictures very similar to those here presented are reproduced in many of the works of radiology, particularly in connection with large tumours of the head of the pancreas, and there are suggestions in many textbooks of medicine that pressure from a distended lesser sac may so affect the stomach that the x-ray picture will show a large filling defect. There are few reproductions, however, of stomach plates which show such inability of the cardiac end of the stomach to push its barium contents down into the lower two-thirds of the organ, and it was doubtless the absence of peristaltic movements and failure of the barium to be deposited below the cardia which induced consultants to think that the pictures represented an inflammatory oedema of the stomach walls. True inflammatory condi-

tions of such extent must certainly be rarely seen and the error might be held excusable. One notes that the senior resident, Dr. Carveth, early made the suggestion that the obstruction might be due to a collection in the upper abdomen, probably in the lesser sac, pressing forward and actually preventing the barium from descending. "The barium," he notes in one observation, "is still retained in the cardiac end of the stomach after 24 and 48 hours, while below this there was at one time a fluid wave which could not be made to mix with the barium in the cardia, possibly," he states, "due to a collection in the lesser sac." Since at the autopsy 500 c.c. of blood-stained fluid was found in the lesser sac, and there was free connection with the duodenum allowing the entry of air into the sac, the obtaining of such a fluid wave by palpation of the epigastrium might well be possible.

A careful autopsy made by Dr. Lougheed went far to explain the nature of the peculiar radiological findings. There was a small amount of free bloody fluid in the general cavity of the peritoneum; the gall bladder was enlarged and inflamed. The left lobe of the liver was adherent to the lesser curvature of the stomach. The foramen of Winslow was blocked by the inflammatory process, which had involved the left lobe of the liver and the stomach. There was no true ulceration of either the stomach or duodenum. The head of the pancreas had degenerated into a small necrotic mass, the body and tail of this organ being the seat of a haemorrhagic inflammation throughout which areas of necrosis were in evidence. From the head of the pancreas the necrotic process had eaten through the duodenum, completely destroying the diverticulum of Vater, and there was another perforation from the head of the pancreas into the lesser sac. Through these two perforations the contents of the lesser sac flowed freely into the duodenum. The posterior wall of the stomach reaching up to the lesser curvature was thinned and showed the effects of the necrotizing action of the fluid in the lesser sac. No distinct thickening of the walls of the stomach or duodenum was anywhere to be noted.

The conclusion to be drawn from the findings at operation and autopsy in this most tragic case, more particularly as affecting the stomach, would seem to be that both pressure from the accumulated fluid in the lesser sac and partial or complete paralysis of the musculature of the lower half of the stomach were preventing the deposition of the barium in this area.

In most of the standard works on radiology one sees references to the distortion of the stomach picture produced by tumours surmounting the kidney. One finds little or nothing, however, on the question of stomach defects caused by the falling forward of a suprarenal tumour as the patient lies on his stomach.

References to filling defects in the stomach caused by pressure of large tumours of the head of the pancreas are also readily found. One finds nowhere, however, any suggestion that

filling defects due to accumulation of fluid in the lesser sac have been observed or pictured; displacement of the stomach downwards, and as a whole, is usually reported.

## CARCINOMA ORIGINATING IN SEBACEOUS CYSTS

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THE occurrence of carcinoma within a sebaceous cyst is still of sufficient rarity to justify the report of several additional cases. Ricker and Schwalbe,<sup>15</sup> in 1914, were able to collect 43 examples from the literature. Caylor<sup>6</sup> has reported the largest individual series up to the present time. It consisted of 12 instances (3.44 per cent) which occurred in 236 sebaceous cysts derived from the large volume of pathological material available at the Mayo Clinic. Bishop<sup>1</sup> examined 119 sebaceous cysts and found 11 (9.2 per cent) which had carcinoma present. Stone and Abbey<sup>19</sup> found 8 malignancies (2.2 per cent) in a group of 363 specimens examined. These four reports are the largest series yet to be recorded. The remaining contributions to the literature are mainly isolated case reports.

TABLE I.  
SUMMARY OF DATA PUBLISHED IN THE LITERATURE\*

SEX (84 cases):

Males.....	42	50.00%
Females.....	37	44.00%
Sex not stated.....	5	5.95%

AGE (33 cases):

Average age in 33 patients.....	58.8 years
Average age in 15 males.....	58.0 "
Average age in 18 females.....	58.8 "
As reported by Caylor <sup>6</sup> .....	58.0 "
As reported by Bishop <sup>1</sup> .....	64.2 "
As reported by Stone and Abbey <sup>19</sup> .....	47.5 "

AVERAGE KNOWN EXISTENCE OF SEBACEOUS CYST  
(20 cases):

Males.....	12	10.8 years
Females.....	8	8.0 "

LOCATION OF SEBACEOUS CYST (58 cases):

Scalp.....	20	34.50%
Eyelids.....	9	15.51%
Nose.....	9	15.51%
Forehead.....	8	13.80%
Cheek.....	6	10.35%
Neck.....	1	1.72%
Shoulder.....	1	1.72%
Arm.....	1	1.72%
Abdominal wall.....	1	1.72%
Back.....	1	1.72%
Knee.....	1	1.72%

(Note: 53 (91.4%) were situated cephalad to the shoulders.)

Table I presents a summary of the available data as presented in the accessible literature upon this subject, totalling 84 instances of this pathological entity. The inferences to be drawn from the summarized data in Table I are as follows. Sex is of little significance. The patients are elderly, averaging 57.5 years of age. In 20 instances the average known existence of the sebaceous cyst had been 8.7 years. In 91.4 per cent of all of these malignant sebaceous cysts they were located upon the head or neck. In 40.0 per cent of the patients it was necessary to perform two or more operations so as to completely remove the lesion. In 34 of the reported cases, 14.7 per cent were basal-cell epitheliomas, but none of them arose from a sebaceous cyst

TABLE I.—Continued.

NUMBER OF OPERATIONS PERFORMED IN ATTEMPT TO CURE THIS DISEASE (20 cases):

	Males	Females
Patient refused surgery.....	1	5.0%
One.....	9	55.0%
Two.....	1	20.0%
Three.....	2	15.0%
Four.....	1	5.0%

PATHOLOGICAL FINDINGS (34 cases):

	Deaths	Mortality
Basal-cell carcinoma (None reported upon scalp).....	5	14.7% 0 0.00%
Epidermoid carcinoma:		
Not classified.....	8	23.5% 3 37.50%
Group I, Broder's Classification.....	10	29.4% 0 0.00%
Group II, Broder's Classification.....	4	11.7% 0 0.00%
Group III, Broder's Classification.....	4	11.7% 1 25.00%
Group IV, Broder's Classification.....	1	2.9% 1 100.00%
Pre-cancerous lesions....	2	5.9% 0 0.00%

RESULTS OF CLINICAL FOLLOW-UP (34 cases):

Well.....	24	70.60%
Not traced.....	3	8.82%
Died (7 cases):		

From carcinoma of sebaceous cyst.....	5	14.71%
From other causes.....	2	5.88%

\*Based upon reports by Nos. 1, 4, 5, 6, 12, 13, 15, 16, 17 and 19.

situated in the scalp. This is of interest as a study of 58 of the reported malignant cases showed that 34.5 per cent had occurred in the scalp. Of the 5 cases of epidermoid carcinoma which were graded III and IV, according to Broder's classification, 40 per cent died from recurrence. Fourteen cases were graded I or II, and no deaths were attributable to a recurrence of the carcinoma. In a clinical follow-up study made upon 34 of the patients 70.6 per cent were well; 14.7 per cent had died from recurrence of the epithelioma; 8.8 per cent could not be traced; and 5.8 per cent had died from causes unrelated to their previously removed malignant sebaceous cyst.

Bishop,<sup>1</sup> Broders,<sup>2</sup> Caylor,<sup>6</sup> MacCarty,<sup>10, 11</sup> Ormsby,<sup>14</sup> Stelwagon,<sup>18</sup> and the Suttons<sup>20</sup> have adequately and thoroughly discussed the origin of sebaceous cysts, and have enumerated the various factors responsible for their malignant degeneration. These excellent data will not be

**CASE 1**  
A Mexican male, aged 40, a labourer, entered the minor surgical clinic complaining of a tumour on the anterior abdominal wall which had become painful and was enlarging in size. He had noticed this mass about four years previously. Examination showed this to be cystic, measuring 2 x 2 x 1.5 cm., situated in the right lower anterior abdominal wall, which was rather firm and irregular to palpation. It was completely removed under local anaesthesia. Microscopic sections revealed the presence of an epidermoid carcinoma, grade II, growing profusely within the walls of a sebaceous cyst. Caylor found two cases (0.87 per cent) of his series of 236 instances that occurred in this same area; while one (0.43 per cent) became malignant and was diagnosed as a squamous-cell epithelioma, grade I (Case 6 of his series of 12 malignant sebaceous cysts). Fig. 1 depicts a typical area from the cyst wall showing the carcinoma.

#### CASE 2

A German male, aged 77, a farmer, had had a "wen" on the right side of his face for the previous seven years which periodically drained foul-smelling cheesy material. This had been cauterized by his own physician seventeen months previously. The area failed to heal entirely, and four months ago the ulcerated area began to enlarge and became indurated. When first seen the ulcerated lesion measured 3 x 3 x 1 cm., and appeared clinically to be unquestionably malignant. The entire lesion was treated by wide excision and thorough diathermy. Microscopic examination of the specimen re-

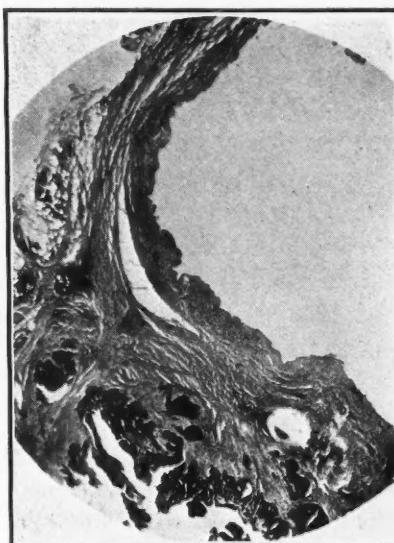


Fig. 1

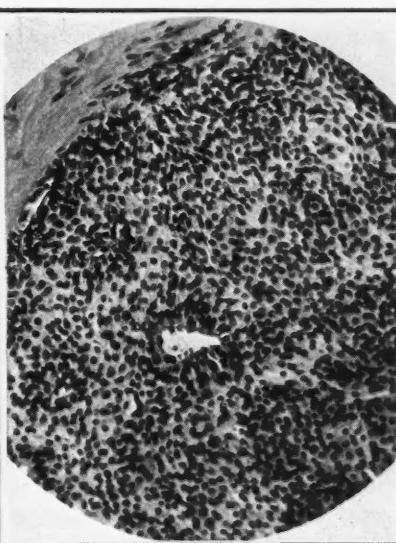


Fig. 2

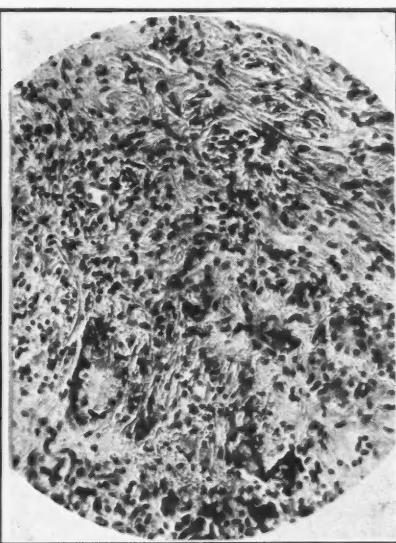


Fig. 3

**Fig. 1.** (Case 1).—Shows the presence of an epidermoid carcinoma, grade II, in the wall of a sebaceous cyst. (x13). **Fig. 2.** (Case 2).—Shows the histological details of the epidermoid carcinoma, grade III, in the wall of a sebaceous cyst. (x100). **Fig. 3.** (Case 3).—Shows definite precancerous changes in the walls of a sebaceous cyst. (x130).

repeated here. However, the reader is urged to read at his leisure the classical contribution of Caylor upon this subject. Nothing has been added to the sum of our knowledge upon this subject during the past eleven years since the publication of his article.

I wish to report briefly three examples of this pathological condition that have occurred in the routine examination of approximately 9,000 pathological specimens (0.033 per cent).—

vealed an extensive epidermoid carcinoma, grade III, in the remnants of a sebaceous cyst. Fig. 2 is a photomicrograph of the histological appearance of the epidermoid carcinoma.

Caylor had 12 (14.71 per cent) sebaceous cysts in this location in his group of cases, and two (0.87 per cent) were malignant, being graded II and IV, respectively. (Cases 7 and 12).

#### CASE 3

An Austrian male, aged 45 years, entered the minor surgical clinic complaining of a cystic tumour in the palm of his left hand, situated between the second and

third metacarpals, of about five months' duration. This mass, although painless, interfered with his working as a labourer and had recently slightly enlarged in size. Under local anaesthesia, this cyst was removed in its entirety. Microscopic study revealed the presence of areas of atypical epithelial cells containing large hyperchromatic nuclei and enlarged nucleoli with an occasional mitotic figure. This microscopic picture was diagnosed as being a definite precancerous lesion in a sebaceous cyst wall. Fig. 3 is a photomicrograph demonstrating the precancerous histological appearance of the sebaceous cyst wall.

According to the Caylor series, one cyst (0.43 per cent) occurred on the palmar aspect of the left second finger, and this lesion was benign. No cases of malignant degeneration were found recorded in the literature as occurring in this location. Bishop included two instances of precancerous changes in sebaceous cysts of the scalp in his article.

#### SUMMARY

Three instances of malignant changes occurring in sebaceous cysts are recorded. The literature has been partially reviewed and the data obtained from this study have been tabulated. All sebaceous cysts should be considered as precancerous lesions, and they should be closely observed if the individual does not consent to their surgical removal. Increased age, long existence of the sebaceous cyst, and probably local irritation are important contributory factors in the causation of malignant changes in sebaceous cysts. These three reported instances occurred

in some 9,000 routine examinations of all types of pathological material, an incidence of about 0.033 per cent.

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#### MYASTHENIA GRAVIS: RESULTS OF TREATMENT IN SIX CASES\*

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AS early as 1870 Rosenthal<sup>1</sup> pointed out that certain myopathies were associated with disturbances in creatinine excretion. In 1909, Levene and Kristeller<sup>2</sup> carried out quantitative studies on cases with myopathies which showed a definite disturbance in creatine and creatinine excretion, namely, that there was not only a low creatinine but a high creatine excretion in these cases. In 1929, Brand, Harris, Sandberg and Ringer<sup>3</sup> showed that when glycine was fed to patients with progressive muscular dystrophy there was a definite increase in the excretion of creatine. Thomas, Milhorat and Techner<sup>4</sup> (1932) repeated this work and confirmed it, but, having carried on the experiments over a prolonged

period, they observed the therapeutic effects of such administration in cases of progressive muscular dystrophy. Others<sup>5</sup> claim similar results. Boothby<sup>6</sup> found no clinical improvement when glycine was administered to three patients with progressive hypertrophic muscular dystrophy. However, he did note a marked improvement on giving glycine to two patients with myasthenia gravis, although a third improved very little. Since this report many other workers have confirmed the observation that myasthenia gravis is more likely to respond to glycine than other myopathies.

X-ray irradiation of the thymus gland in the treatment of myasthenia gravis was used by German workers as far back as the beginning of the century. Pierchalla<sup>7</sup> in 1921, referred to

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the various opinions as to its merits. This method of treatment has been advocated by a number of observers since that time. However, others have doubted its value on the grounds that the remissions attributed to treatment in certain cases may have been spontaneous in nature.

In 1929, Edgeworth,<sup>8</sup> who is suffering from myasthenia gravis, found a marked improvement of her condition with the use of ephedrine, and since then many other favourable reports have been made concerning the use of this drug in myasthenia gravis.

Walker<sup>9</sup> (1934) was impressed by the similarity in manifestations of curare poisoning and myasthenia gravis. Because physostigmine is a partial antidote for curare poisoning, she felt that it might prove of benefit to patients with myasthenia gravis. Having an undoubted case of myasthenia gravis under her care, she administered physostigmine and obtained very definite improvement in the symptoms. It was necessary to combine atropine with the physostigmine to combat the intestinal cramps. Denny-Brown<sup>10</sup> (1935) advises 20 min. of tincture of belladonna in water by mouth, followed twenty minutes later by 1/6 gr. physostigmine salicylate in water, administered once daily on an empty stomach. This, the writer states, causes a decrease in the symptoms of myasthenia. Recently, an isomer of physostigmine, called prostigmine, has been prepared, which is more active and not so prone to produce intestinal colic. The effect of this drug on cases of myasthenia gravis is very dramatic, but, unfortunately, of short duration. This preparation may throw some light on the pathology of myasthenia gravis. It is now postulated that the effect of prostigmine is to inhibit the acetylcholine esterase in the muscle cell at the nerve ending and thus allow the acetylcholine to act upon the muscle cell.\* Whether the increased stimulation of the muscle cell proves beneficial or harmful ultimately remains to be seen by further use of protigmine.

Simon<sup>11</sup> recently reported the successful use of antuitrin in two cases of myasthenia gravis, but as yet this work lacks confirmation.

#### CASE HISTORIES

Since 1930 six cases of myasthenia gravis have been admitted to the public wards of the Toronto

\*In this connection, Drs. McVicar and Cleghorn, of the Department of Medicine, estimated the activity of the acetylcholine esterase in blood in three of our patients (Cases 1, 5 and 6) and found no consistent deviation from the normal amount of this substance in the blood.

General Hospital. Several other cases observed during this period have not been included because the diagnosis of myasthenia gravis was not sufficiently definite. These six cases have been under the continuous observation of the author, and their clinical progress has been studied both in hospital and subsequent to discharge in the out-patient clinic. The clinical histories which follow are reported in some detail with particular reference to the effect of the various therapeutic agents employed.

#### CASE 1

Miss V. K., aged 21, factory worker, admitted to the Toronto General Hospital, October 14, 1931.

*History of illness.*—Three years before admission she noted weakness of her legs, particularly when attempting to mount steps. The weakness became more apparent towards the latter part of each day and was much less noticeable in the morning. By December, 1929, it became necessary to stop working, and about this time double vision developed after reading. During the six months previous to admission phonation became weak after conversing a short time. She had difficulty in chewing, and as each meal progressed swallowing required increasing effort. Her symptoms have always been much worse during the week preceding each menstrual period. At this time the weakness in her legs and back had become so severe that she had had to crawl upstairs on hands and knees. Her condition always improved quite markedly on the third day of the menstrual flow.

*Examination.*—The patient was a well-nourished girl with no muscular wasting. There was moderate bilateral ptosis; the lips were constantly parted, and it required obvious effort on her part to bring them together. Frequently she would support her lower jaw with her hands. No strabismus was demonstrable, but diplopia was readily produced. Extreme upward, downward, lateral movements or convergence could only be maintained momentarily. The voice was nasal, and after conversing for a few minutes it became weak and indistinct. The muscles of the trunk and limbs were all very weak, especially those of the lower limbs and trunk, and sustained effort against resistance of the various muscle groups resulted in rapid fatigue. After resting for a few minutes the power improved. Her gait was slow and of a waddling character. She was unable to walk upstairs unaided. When placed recumbent on the floor she was unable to raise herself without assistance. Apart from these findings, examination revealed nothing of significance except the blood pressure, which was 94/62 reclining, 86/62 sitting up. X-ray and fluoroscopic examination of the thymus gland revealed no enlargement. Electrical stimulation with the faradic current showed the fatigue phenomenon in the muscles of the face and limbs characteristic of myasthenia gravis.

*Treatment and progress.*—The patient was placed at rest in bed for six weeks and given a course of x-ray irradiation to the thymus gland. She was discharged from hospital in November, 1931, unimproved. A slight improvement was noted during January and February, 1932, but in March a very decided improvement occurred. This continued until September and during the summer she was able to take fairly long walks and to eat without any weakness developing. However, in September, 1932, she began to tire more easily and difficulty in swallowing recurred. The weakness in her limbs became increasingly severe and on-re-admission to hospital in January, 1933, her body showed numerous bruises from falls sustained due to weakness in the legs. Examination at this time showed ocular muscles weak and easily fatigued, resulting in strabismus and diplopia. Ocular convergence was a weak movement which could not be maintained. There was generalized severe weakness of all facial muscles on voluntary or emotional movements. Attempts to chew

or swallow resulted in rapid fatigue of the muscles concerned. The voice was nasal but did not fatigue as readily as formerly. The power in the muscles of all four limbs was poor, particularly in the proximal groups. The patient had great difficulty in sitting up from a recumbent posture, even when using her arms.

On January 24, 1933, glycine 5 grams thrice daily, and, twenty minutes after each dose, ephedrine,  $\frac{1}{4}$  grain, were prescribed. During the next three days a remarkable improvement occurred. On January 27 she could eat her meals without difficulty, could step up on to a chair, and was free of strabismus or ptosis even at the end of the day. She noted a subjective increase in muscular power and stated that she felt stronger than at any time since the commencement of her illness. Examination substantiated this statement and it was only after prolonged repeated movements that fatigue could be produced.

In April glycine was discontinued for two weeks. A few days after stopping glycine, the patient noted that she tired more easily. Her face assumed its former appearance, with well-marked ptosis and diplopia and profound weakness of all muscles: chewing, swallowing and speech were affected. When the glycine was resumed there was rapid improvement in the power of her limbs and the muscles of expression and mastication. The diplopia improved very slowly, however. On a day when she felt exceptionally well a duodenal tube was passed for experimental reasons. Although this did not distress her much at the time, extreme weakness developed in a few hours. Her condition gradually became worse and she was so weak the following day she could hardly move her limbs; her face was very myasthenic in appearance, and she complained of headache and vomited several times. The weakness persisted for three weeks, and then gradually recovery occurred so that she was discharged from hospital in July.

During the summer she felt generally well. She could walk fairly long distances, could climb stairs, and had no trouble eating her meals or in talking. Occasionally she experienced diplopia. In September a duodenal tube was passed again, but this time a stylet was used to avoid any effort of swallowing on her part. No ill effects resulted from this procedure. During the winter the patient remained well for the most part, but on occasions one or other of her symptoms would return for a brief period. From February to May, 1934, she was exceptionally well. She could walk two miles without fatigue, could sew for long periods without any weakness of eyes or hands occurring; she had no trouble in eating or talking. The myasthenic appearance of her face almost entirely disappeared. However, in May she had a recurrence of transitory symptoms such as she experienced during the winter. At this time the glycine was increased to 10 grams three times daily, and the ephedrine reduced to  $\frac{1}{8}$  gr. three times a day. Her condition became slightly worse during the next twelve days. Accordingly, the ephedrine was increased to  $\frac{1}{4}$  gr. three times daily. This dose of ephedrine in combination with glycine proved the most effective. The patient's condition gradually improved, and, with the exception of the week preceding each menstrual period, during which her symptoms always became much worse, she was able to get about and do things for herself with no marked difficulty in chewing, swallowing or reading. However, she was not able to resume ordinary activity at any time.

In March, 1935, glycine and ephedrine were stopped for four days, with rapid and severe recurrence of all symptoms. When the patient was prostrated, prostigmine, 2.0 c.c., and atropine, 1/100 gr., were given subcutaneously. Rapid and marked improvement in the power and ability to withstand fatigue of all the affected muscles was observed, but she complained of a "tight feeling" in the eyes, nausea and nervousness. The beneficial effect had completely worn off within three hours after the injections, and she felt rather worse than before prostigmine was administered. Subsequently, the patient was given physostigmine salicylate in doses varying from 1/24 to  $\frac{1}{8}$  gr., three times daily, with tincture of belladonna in varying doses accompanying each dose of physostigmine. This treatment proved ineffective and her myasthenia

became very severe. On small doses of physostigmine and ephedrine,  $\frac{1}{4}$  gr. three times a day, she was a little improved but never so well as when taking only glycine 5 grams and ephedrine  $\frac{1}{4}$  gr. three times a day, which was accordingly recommended.

Beginning on July 5, 1935, the patient was given nine daily intramuscular injections of antuitrin, 1 c.c., with no improvement whatever. During August she was taking glycine and ephedrine as formerly prescribed and leading a very restricted life at home. Providing she did not over-exert herself she was moderately comfortable. Commencing on September 23, three days after the onset of menstruation, the patient was given daily subcutaneous injections of prostigmine, 2 c.c., and atropine, gr. 1/150. At this time in the menstrual cycle patient usually feels at her best. Glycine and ephedrine were continued as formerly and she was given sedatives at night to ensure adequate sleep. Six injections were given in all, and following each she experienced a marked beneficial effect which lasted three to five hours, but the increased strength was less marked following the last two injections than it had been after the first four. On September 26 she had to go to bed six hours after the injection because of extreme weakness. On September 27 the weakness, after the effect of the injection wore off, was even more severe and she had great difficulty in walking on the following morning. On September 29 it was decided to discontinue the injections because she was almost unable to stand or use her arms, and the muscles of her eyes and face were very weak; mentally her perceptions were dulled and she complained of difficulty in thinking. The condition of extreme muscular fatigue lasted until October 4 and then gradually over a period of four weeks she regained her former strength while taking glycine, 10 gm., and ephedrine,  $\frac{1}{4}$  gr., three times a day. She has continued to take this medication up to the present time and is able to lead a moderately comfortable although restricted life.

The patient's blood pressure readings and heart rate and rhythm, together with the effect of posture, were recorded before and after prostigmine had been administered and showed no essential difference. Repeated blood pressure readings showed the following range: erect, 88/58 - 80/58; recumbent, 96/66 - 86/62. The pulse rate always increased in rapidity when the patient assumed the erect posture. The blood pressure findings were interpreted as indicative of postural hypotension. Whether erect or recumbent, examination of the apex beat revealed an irregularity of rhythm characterized by slowing and accelerating, alternatively and irregularly, independent of respiration. Examination of the heart, including an electrocardiographic record, was otherwise negative. The absence of any change in the above findings after prostigmine had been administered suggests that the postural hypotension in this case is independent of the myasthenia gravis.

#### CASE 2

Mr. D. T., aged 31; occupation, foreman; admitted to Toronto General Hospital July 27, 1931.

*History of illness.*—Four years previously friends of the patient observed that his right eyelid drooped towards evening. Since that time this had occurred daily although never in the morning. Two years before admission he experienced diplopia for a period of six weeks. This was not constant, but came on after he had been using his eyes for some time and always disappeared with rest. Four months after the diplopia subsided his voice commenced to weaken towards evening, and at this time his speech would sometimes be so indistinct that it was difficult to make himself understood. About the same time difficulty in swallowing food developed half way through each meal. The food became arrested against the roof of his mouth and it was often necessary to use his fingers to push it along. The ptosis, dysarthria and dysphagia continued until the time of admission, becoming increasingly severe, and later were accompanied by a feeling of tiredness in his arms and legs which developed each afternoon during work.

*Examination.*—A man of fair physique with no muscular wasting. There was a moderate ptosis of the

right upper eyelid, which increased during the examination. The facial muscles were all very weak, giving the face a smooth, ironed-out appearance. He was totally unable to purse his lips for whistling. On showing the teeth or smiling, there was very little retraction of the corners of the mouth. The orbicularis oculorum were so weak that he could offer scarcely any resistance to attempts to open his eyes. Observation of the patient while he was eating showed that after chewing solid food for a few minutes the movements of the jaws became increasingly weaker and required more effort on his part, until chewing ceased altogether. Swallowing, likewise, became increasingly difficult and violent attacks of coughing occurred as a result of food entering the larynx. Occasionally fluids regurgitated through his nose. His speech had a nasal quality constantly, but at the commencement of conversation was clear and intelligible. After giving part of his history the nasal quality increased and syllables became slurred, until finally the words were almost unintelligible. After resting his voice for about half an hour the patient could speak clearly once more. The power in his limbs was good at the beginning of the examination, but repeated movements of any of his limbs against resistance resulted in gradual fatigue from which they recovered after a period of rest. Neurological examination was otherwise negative. Faradic stimulation showed the characteristic fatigue phenomenon in certain muscles of the face and limbs.

*Treatment and progress.*—The patient was given a course of x-ray irradiation to the thymus gland. A few days after the first treatment improvement was noted, and on discharge from hospital, August 9, 1931, the dysphagia and dysarthria were much less quickly induced and he felt generally stronger in his limbs. The ptosis, however, was unchanged and the facial muscles were still very weak. Improvement gradually continued after discharge so that by October he was able to return to work. At this time there was no tendency to dysphagia or dysarthria, and the ptosis, when present, was very slight. By July, 1932, his facial expression was almost normal. The voice, although slightly nasal, could not be fatigued and his limbs did not tire even after a hard day's work. He continued in good health until January, 1933, when he noted a recurrence of ptosis of his right eyelid towards evening of every day.

Ephedrine,  $\frac{1}{4}$  gr. three times daily, failed to benefit him and was discontinued after several weeks. In September, 1933, he tired easily and had difficulty in chewing towards the end of each meal. In December, these symptoms became worse and he suffered from blurring of vision. In January, 1934, walking became difficult because his right leg tired very quickly. Examination on January 15, 1934, showed the patient with his head far back to compensate for a marked ptosis of his right eyelid. No diplopia or strabismus could be demonstrated, but on rapidly moving his eyes a few times an instability of the ocular movements was noted and he complained of objects being blurred. All voluntary and emotional movements of the face were extremely weak. The voice was nasal but could not readily be fatigued. The right hand grip was much weaker than the left, and fingers four and five of the right hand were particularly weak. On testing with repeated movements against resistance the right upper and lower limbs tired in about half the time required to tire the corresponding limbs on the left side.

On February 1, 1934, glycine, 5 grams three times a day, was prescribed. Improvement occurred rapidly and within one week strength had increased in his limbs, blurring of vision had disappeared, as had also the difficulty in chewing and swallowing. The voice became less nasal and developed more cadence. Improvement continued until August, 1934, when he was practically symptom-free. The only physical sign at the present time is a narrowing of the right palpebral aperture due to a slight ptosis which remains constant and does not alter as formerly. The patient is continuing with the glycine treatment and has suffered no recurrence of symptoms up to the present time (April, 1936).

### CASE 3

Miss D. B., aged 17, admitted to Toronto General Hospital, June 28, 1932.

*History of illness.*—In June, 1930, the patient noticed increasing fatigue towards the end of each day. A few months later she experienced diplopia on attempting to read or sew, which disappeared after resting her eyes. At this time she suffered also from difficulty in chewing and swallowing, which developed half way through each meal and increased as she continued eating. Her voice gradually weakened when she conversed for any length of time. These symptoms all became progressively worse, and during the six months previous to admission she experienced a number of terrifying attacks. These occurred independently of any exertion and consisted of severe palpitation, dyspnoea and fear of impending death. Her mother stated that she became very blue during the attacks, but never lost consciousness, and in about fifteen to thirty minutes the symptoms would slowly pass off.

*Examination.*—Examination showed a poorly nourished young girl, with moderate ptosis of both upper eyelids, and very little play of expression due to severe weakness of the facial muscles. At the commencement of the examination of the eyes there was a slight divergent strabismus present, with some limitation of conjugate movement upwards and to the right. After about five minutes of testing the ocular movements a complete external ophthalmoplegia developed. Following a rest, the ocular movements gradually recovered, although never to a full range of movement. Both emotional and voluntary movements of the facial muscles were very weak and rapidly fatigued with repeated testing. The orbicularis oculorum were so weak that patient could not completely close her eyes. When requested to show her teeth, there was scarcely any retraction of the corners of the mouth, merely a curling of the upper lip. When she attempted to open the lower jaw against resistance the response was very feeble. The voice was high-pitched and weak. When requested to repeat the alphabet she became unable to articulate half way through the fourth repetition, but after ten minutes' rest was able to continue again. The limbs, although generally weak, were not readily fatigued. The gait was not disturbed. Neurological examination, apart from the above findings, revealed no abnormality. Faradic stimulation showed the fatigue phenomenon in the facial muscles characteristic of myasthenia gravis.

*Treatment and progress.*—The patient was kept in bed at complete rest and given ephedrine,  $\frac{1}{2}$  grain three times daily for two weeks. The only improvement noted was in her ability to masticate solid food. She was given a course of x-ray irradiation to the thymus gland, the last treatment on August 6, 1932. From the time of the first treatment progressive improvement was noted, despite the nausea and vomiting which occurred on each occasion. On August 23 she was able to eat well; her voice was much stronger and less easily fatigued; the ptosis was less marked.

A second course of x-ray irradiation was given in September, 1932. Improvement continued, and by October 26, 1932, she felt much stronger and could eat anything without difficulty; her voice did not fatigue with ordinary use; the eyes showed only a slight convergent strabismus even when fatigued but conjugate deviation to the left was incomplete. The ptosis was slight and only occurred late in the day. There had been no recurrence of the attacks with cyanosis and palpitation since admission to hospital.

A further course of x-ray was administered late in November, 1932. Her condition during December showed slight but gradual improvement, although she was still unable to resume ordinary activity. Examination on February 28, 1933, showed that voluntary and emotional movements of the face were all fairly strong; ptosis was absent. She had gained ten pounds in weight in the past four months. The eye movements were full, except for slight weakness of left external rectus, and she experienced diplopia on looking to the left; this became worse after using the eyes, as when walking on busy streets.

Two tablespoonfuls of gelatin, three times daily, were prescribed but during the next three weeks her condition remained essentially unchanged. The gelatin was stopped March 31, 1933, and she was given glycine, 5 grams three times a day. Within a few days the ocular condition improved and she became free of diplopia, only experiencing slight blurring of vision on looking to the left after prolonged use of the eyes. In August, 1933, she was entirely symptom-free and secretly got married. She became pregnant in September, 1933, and during the entire pregnancy felt quite well and had no recurrence of symptoms until April 16, 1934, at which time her sleep was disturbed due to pains associated with the pregnancy. Her expression became slightly myasthenic and diplopia returned on looking to the left. She was admitted to hospital and placed at complete rest in bed until labour commenced.

The glycine was increased to 10 grams three times a day, and sedatives were prescribed at night. Her symptoms cleared up completely after two nights' good sleep. It was found that she was as well on 5 grams of glycine three times a day as on the increased dosage, and the former amount was resumed. On May 6, 1934, the membranes ruptured and she went into labour May 9, at 1.45 a.m. The pains were strong and continued regularly until delivery with low forceps at 7.30 a.m.; the baby weighed seven pounds. Apart from some cyanosis of lips and finger-tips, the patient was in good condition after delivery and showed no myasthenic symptoms. Her pulse rate was 116 per minute four hours after delivery, but gradually became normal in four days. The puerperium was uneventful. She returned home May 22, 1934, and, disregarding advice, soon became pregnant again. She continued taking ephedrine and glycine until April 1, 1935, at which time she stopped it against advice because she felt so well. Her second child was born on May 16, 1935. She suffered no ill effects and has had no recurrence of symptoms. She has taken no medicine of any kind since April 1, 1935, and when last seen in September, 1935, was symptom-free, doing all her own housework and looking after her two children.

#### CASE 4

R. M., aged 21, a truck-driver, was admitted to Toronto General Hospital, July 20, 1934.

*History of illness.*—Two years before admission the patient noted a drooping of the left upper eyelid. The ptosis became manifest during the late afternoon of each day and gradually increased until bedtime. The condition completely disappeared after about two weeks and did not recur until three months before admission to hospital. On this occasion, it was accompanied by a similar drooping of the right upper eyelid, and later there was difficulty in rotating the eyes. He complained of a general weakness and rapid fatigue after any exertion.

*Examination.*—Examination in hospital showed variable ptosis of both eyes, worse towards evening, and greatly improved after rest. An almost complete external ophthalmoplegia was present at times, although, following rest of the eyes, a variable amount of lateral movement of both eyes was usually present, but upward or downward movement was never possible. Marked weakness of both orbicularis oculorum was found on testing. The pupils were moderate in size and reacted well to light and on accommodation. No other abnormalities were found on physical examination. Laboratory investigations, including blood, cerebrospinal fluid and x-ray of skull, were negative.

*Treatment and progress.*—The patient was given glycine, 10 grams, and ephedrine,  $\frac{1}{4}$  gr., three times daily, but at the end of one month no improvement had occurred. The ocular signs showed considerable variation in degree of severity, but no more than before commencing treatment. The glycine and ephedrine were discontinued and the symptoms remained unchanged. On September 12, 1934, glycine, 10 grams three times a day, was recommenced and continued for two weeks with no perceptible effect. On September 26, glycine, 15 grams in saline, was given intravenously and continued once daily until October 13. The patient experienced considerable sub-

jective general improvement in strength, but little objective change was evident. Commencing October 28, 1934, a course of x-ray irradiation to the thymus gland was administered. The patient was discharged from hospital on November 18, 1934, without any definite change having occurred. About the middle of December he commenced to feel better and this improvement gradually continued. He recovered a considerable degree of lateral movement of both eyes and the ptosis was less easily produced and less severe. On April 26, 1935, physostigmine, 2 c.c., and atropine, 1/150 gr., were given subcutaneously. Within thirty minutes ptosis had completely disappeared and power in the orbicularis was much greater. The range of ocular movement increased in all directions, including upwards, but a full range of movement in any direction was not obtained. At the end of two hours the muscles had reverted to their former state. Subsequently no treatment was administered, and in July, 1935, information by letter stated that the patient's ocular movements were continuing to improve gradually. Physostigmine salicylate, gr.  $\frac{1}{8}$ , and tincture of belladonna, 10 min., twice a day, were prescribed. The patient took this treatment regularly for two weeks but abandoned it because there was no apparent beneficial effect and it made him feel nauseated. Seen in October, 1935, ptosis was still present every afternoon but was not so severe nor so readily produced as formerly. On examination at this time, the only limitation in the range of ocular movements was in conjugate deviation of both eyes to the left and in upward movement of the left eye. Power in the orbicularis oculorum was much improved. Patient stated that he felt stronger generally and that his ocular disability now caused him very little inconvenience.

#### CASE 5

C. S., aged 29, mechanic, admitted to Toronto General Hospital November 13, 1934.

*History of illness.*—In 1920 the patient first experienced drooping of the right upper eyelid and diplopia. These symptoms developed towards evening every day and always subsided after rest. Three months after the onset a gradual recovery occurred. In 1927 and again in 1930 the symptoms recurred. On each occasion improvement took place within several months, and during the intervals between relapses he was symptom-free if he did not overstrain his eyes. In 1932 the same symptoms returned more severely than on any previous occasion, and, in addition, his right hand became weak after any strenuous effort. The symptoms persisted and in 1933 the left hand became similarly affected. In May, 1934, the muscles of his jaws tired while eating and swallowing was often difficult. After walking a short distance it became increasingly difficult to raise his feet, and he had several falls going up and down stairs. Both eyelids now tended to droop and diplopia was present most of the time. The symptoms gradually increased so that on admission to hospital he was practically helpless.

*Examination.*—Examination showed a poorly nourished man with partial ptosis of both upper eyelids, more marked on the right side. The range of movements of the eyes was limited in all directions, but the degree of limitation was to some extent variable, depending on the amount of rest prior to the test. With repeated testing a complete external ophthalmoplegia could be produced. The facial muscles were all extremely weak, particularly the orbicularis oculi. The patient was unable to open the lower jaw against slight resistance. Following a few minutes' conversation, the voice became weak and nasal. The muscles of the trunk were all very weak and he was unable to sit up in bed without using the arms, or to rise to his feet from a recumbent posture on the floor. The upper limbs were weak at all joints, the greatest weakness being in the fingers of both hands. These could not be fully extended or completely flexed voluntarily without a long period of preliminary rest. Power in the lower limbs was less impaired than in the arms. The greatest weakness was in the ankles. After walking a distance or voluntarily flexing and extending the feet at the ankles a number of times a degree of bilateral foot drop would

become apparent, and dorsiflexion of the feet at the ankles would become very weak. Strength in the muscles gradually returned after a period of rest.

Apart from the above findings, examination was essentially negative. The muscles of the limbs were flabby but no localized wasting was present. The tendon reflexes were all present and equal on the two sides and could not be fatigued. The affected muscles showed the fatigue phenomenon characteristic of myasthenia gravis on faradic stimulation.

*Treatment and progress.*—From November 15 to 29, 1934, glycine, 15 grams in 100 c.c. saline, was administered daily intravenously. On November 17 the patient noted increased power in his legs and freedom from difficulty in chewing or swallowing. Objectively the ptosis was less marked. This improvement was maintained with no change until December 1, two days after discontinuing glycine, when he complained of recurrence of difficulty in chewing and swallowing and that his legs tired more rapidly. The ptosis was more quickly induced. The symptoms gradually increased in severity and on December 5 he was worse than on admission to hospital. On December 7, daily intravenous glycine was resumed, with improvement commencing on the following day. From December 10 to 12 glycine was omitted unknown to the patient and saline alone given intravenously. The symptoms had all recurred by December 12 and the patient suggested that a bad lot of medicine was being used. He stated that a tingling sensation in certain muscles, previously always present following each injection, had not been perceptible after the last three injections. Intravenous glycine was once more resumed and gradual improvement occurred as before. The voice and facial expression also improved on this occasion. Following discontinuance of glycine intravenously the symptoms returned. A few days later glycine, 10 grams three times a day per os, was prescribed. Rapid improvement occurred in the power of the limbs and facial muscles. The ptosis became less frequent and less severe, difficulty in chewing and swallowing disappeared, and the range of ocular movements increased. Within a few minutes of each dose of glycine he experienced a burning, pricking sensation in certain muscles of the face and limbs lasting about twenty minutes. Subsequently ephedrine,  $\frac{1}{8}$  gr., was given before each dose of glycine and on this treatment further improvement took place. He became able to fully extend his fingers and to make a complete fist without effort. The ephedrine was increased to  $\frac{1}{4}$  gr., three times daily, with steady improvement. A few days later the dose of ephedrine was increased to  $\frac{1}{4}$  gr. five times daily, which produced some further improvement in the power of the facial muscles and the muscles of the limbs. Ephedrine,  $\frac{1}{4}$  grain, six times daily produced symptoms of intolerance after one week. All treatment was discontinued on March 25, 1935, and the following day the patient became very weak with marked ptosis and ophthalmoplegia, gross weakness of the muscles of the limbs and face, difficulty in chewing and swallowing, and great weakness of the voice. Prostigmine, 2 c.c., and atropine, 1/100 gr., were given subcutaneously on March 26 at 2.30 p.m. Within fifteen minutes power in all the muscles commenced to improve, and at the end of one hour the patient looked and acted like an entirely different man. The power in the muscles of the face and limbs improved greatly and the ptosis disappeared. He was able to walk vigorously, bend over without difficulty, and use his hands in normal fashion, freely and with fair power. Ocular movements showed only a little increased range. There was no difficulty in chewing or swallowing and his voice was clear and strong. By 4.30 p.m. the weakness was returning and at 7.30 his condition was as before the administration of the prostigmine. Glycine, 10 grams three times a day, and ephedrine,  $\frac{1}{4}$  grain five times daily, were resumed until April 30, 1935. At this time all other treatment was stopped and patient was given physostigmine salicylate, 1/12 gr., and tincture of belladonna, 10 min., three times daily. His condition became decidedly worse and during two weeks varying doses of physostigmine (gr. 1/6 - 1/24) were tried but without benefit. Finally, glycine, 10 grams three times daily, was given as well as physostigmine and belladonna and

the patient's condition improved gradually. On physostigmine, 1/6 gr. twice daily, belladonna, 10 min. twice daily, and glycine, 10 grams three times daily, the power and fatigability of the muscles of the face, trunk and limbs were only a little less satisfactory than when taking glycine and ephedrine as previously.

From August 16 to 24, 1935, inclusive, he received daily intramuscular injections of antuitrin, 1 c.c. This treatment produced no change in his condition during the period of administration or subsequently. On August 28 all other treatment was stopped and he was given prostigmine, 2 c.c., and atropine, 1/150 gr. subcutaneously. Improvement similar to that recorded previously occurred. This treatment was repeated on August 29 and 30. It was then discontinued because the patient received less benefit with each succeeding dose, and the reaction of fatigue which followed the temporary improvement became increasingly severe. On August 31 glycine, 5 grams three times a day, and ephedrine,  $\frac{1}{4}$  gr. five times daily, were recommended and the patient slowly returned to the same condition as prior to the administration of prostigmine. He has remained on this treatment up to the present time (April, 1936) and recent examination showed less fatigue on chewing and swallowing than when he first came to hospital: meals could be eaten in comfort. The ptosis was much less frequent and severe and the range of ocular movements was generally a little increased. The weakness and rapid fatigue of the upper and lower limbs were very marked and confined the patient to a life of invalidism.

#### CASE 6

Miss G. W., aged 29, typist, admitted to Toronto General Hospital on January 24, 1935.

*History of illness.*—The patient was perfectly well until four years before admission to hospital. At that time her voice commenced to weaken towards evening each day so that it was an effort to make herself understood. Shortly afterwards she experienced difficulty in swallowing the last few mouthfuls at a meal, and occasionally liquids regurgitated through the nose. Later, fatigue of the jaw muscles developed about half way through each meal and gradually increased effort was required to masticate her food. She continued at work until July, 1932, when she noticed weakness of her arms after any sustained effort. Over a period of a few weeks her upper limbs gradually became more easily fatigued until finally she had to stop work. About this time her eyelids commenced to droop towards evening each day, and it became impossible to open them fully or to close them tightly. During the summer of 1933 the muscles of her neck became weak and her head would frequently fall forward. Her legs tired after walking a short distance and her feet dragged with each step. She had difficulty in stepping on and off street-cars. In June, 1934, her symptoms all became very much worse, and she commenced having blurring of vision almost constantly, and diplopia if she used her eyes very much. The weakness in her limbs was so severe that she was confined to bed. Breathing was frequently a great effort and she often feared impending death from inability to breathe.

*Examination.*—Examination at this time showed a poorly nourished girl of average intelligence and emotionally stable. There was bilateral partial ptosis and well-marked weakness of all the facial muscles on emotional or voluntary movement. The power of the muscles of the jaw, neck and limbs was much impaired. Her voice was weak and fatigued rapidly when talking, but recovered with rest. There was no gross strabismus at rest, but on repeated testing of ocular movements definite weakness of the internal and external rectus muscles of both eyes could be produced. Examination of the cranial nerves, limbs and trunk was otherwise negative. Various affected muscles showed the fatigue phenomenon characteristic of myasthenia gravis when the faradic current was applied.

*Treatment and progress.*—The patient was given glycine, 5 grams, and ephedrine,  $\frac{1}{4}$  gr., three times a day, commencing June 25, 1934. This treatment was continued until admission to hospital. The day following commencement of treatment she was much improved in

all respects and able to eat her meals in comparative comfort. After six days there was no difficulty in chewing or swallowing liquids, and no diplopia. She was able to walk short distances and could use her upper limbs for ordinary tasks. However, the facial muscles, although stronger, were still very weak; the voice was nasal and tired rapidly; and the muscles of her limbs would stand no unusual exertion. This condition remained stationary until admission to hospital on January 24, 1935.

Following admission, ephedrine was discontinued and glycine, 10 grams three times a day, was given alone. Her condition became rapidly worse. Ephedrine,  $\frac{1}{4}$  gr. three times a day, produced immediate improvement, and this drug was gradually increased to  $\frac{1}{4}$  gr. six times daily, with remarkable improvement, particularly in the power of the limbs. The glycine was discontinued for several days and then recommenced without the slightest effect on her condition.

On March 25 ephedrine was discontinued and during the next two days her condition became alarming. She developed marked weakness of all the muscles of her face, limbs and trunk, attacks of dyspnoea preventing sleep, great difficulty in chewing and swallowing, and her voice was so weak and nasal she could not be understood. On March 28, physostigmine, 2.2 c.c., and atropine 1/100 gr., were injected subcutaneously. Within twenty minutes striking improvement was observed in the power of the muscles of the face and limbs. This continued for one hour, by which time she was able to walk vigorously, step up on a chair with ease, her facial muscles behaved in almost normal fashion, the voice was clear and strong, although still perceptibly nasal. She ate a large meal with no difficulty whatever. Three hours later, however, her condition was the same as before the injection.

During the next four weeks the patient was given physostigmine salicylate in varying doses from 1/24 gr. to 1/6 gr., with tincture of belladonna. She obtained absolutely no benefit from this medication, whether with or without glycine and ephedrine. Even small doses of physostigmine caused her to be nauseated and the symptoms of myasthenia gravis became much worse. Subsequently she was given ephedrine,  $\frac{1}{4}$  gr. six times daily, only and has continued on this until the present time (April, 1936) with very satisfactory improvement. The facial expression is only slightly myasthenic; there is no ptosis; retraction of the mouth is good; the forehead can be moderately wrinkled; the weakest muscles are the orbicularis oculorum and complete closure of the eyes is not attained. Chewing and swallowing are well carried out, unless exceptional demands are made. There is no diplopia, no weakness of the neck, and no dyspnoea. The upper limbs do not fatigue in ordinary household work. She can walk moderate distances without fatigue and is gaining weight.

#### THE RESULTS OBTAINED WITH VARIOUS TREATMENTS EMPLOYED

There is considerable difference of opinion regarding the value of certain methods of treatment advocated for myasthenia gravis. A number of therapeutic measures were used in all the six cases reported above, and an attempt was made to carefully observe the effect of each. It is well recognized that cases of myasthenia gravis are liable to have spontaneous remissions, and that periodic variations in the severity of the symptoms are to be expected, whether treatment is administered or not. This is well shown in the histories of Cases 4 and 5. For these reasons it is often extremely difficult to estimate correctly the value of treatment, and it is necessary to be on guard against drawing false conclusions.

Whenever possible we repeated our observations several times, studying the effect of withdrawal as well as the changes which occurred following the administration of any therapeutic agent. With the exception of Case 4, the patients in this series had severe bulbar symptoms and the urgency of their condition sometimes forced us to employ several remedies in quick succession, rendering correct evaluation difficult.

The results obtained in this small series of cases will be briefly summarized. The methods of treatment used will be considered separately.

*Glycine*\*.—Glycine per os was given to all 6 patients. The doses varied from 5 to 15 grams three times daily. Symptomatic improvement was observed in 4 patients (cases 1, 2, 3 and 5); no improvement followed the administration of glycine in the remaining 2 patients (cases 4 and 6). Of the patients who benefited, 2 (cases 1 and 5) showed varying degrees of symptomatic improvement within a day or so of commencing treatment, but as quickly returned to their former state whenever the substance was discontinued. However, although definite subjective and objective improvement occurred in these two cases during the administration of glycine, it consisted only in a lessened fatigability of certain affected muscle groups. While the disease was by no means controlled by glycine therapy, these two patients were made more comfortable, and possibly were saved from death by partial relief of their severe bulbar symptoms.

One of the remaining two patients who benefited by glycine (case 3) had already shown marked symptomatic improvement before this treatment was instituted. However, on glycine recovery was much more rapid than previously, and this patient has remained well for two and a half years. That glycine is not essential to maintain this patient free of symptoms is shown by the experience of the past five months, during which time she has taken no treatment and has had no recurrence of symptoms in spite of the strain imposed by childbirth and the entire responsibility of looking after her household.

The remaining patient (case 2) showed more apparent response to glycine than any of the others. His symptoms, which had been progressively increasing for four months, were immediately improved when glycine therapy was commenced. Within five months he became symptom-free. However, this patient recovered from a previous relapse shortly after a course of x-ray treatment to the thymus gland, which would indicate that if glycine had any effect in his recovery it was, at least, not specific.

Dosage was not an important factor in the cases which received glycine. Cases which were symptomatically improved by 5 grams three times daily did not receive greater benefit by increasing the dose. Glycine, 15 grams in 100 c.c. of saline, was administered intravenously daily for a period of several weeks to 2 patients (cases 4 and 5). One (case 5), who also showed some improvement on glycine per os, was apparently helped by intravenous glycine although the effect was not so great as with glycine per os. That the intravenous glycine was of some benefit was indicated by the relapse which occurred when glycine was omitted from the intravenous without the patient's knowledge. The other patient (case 4) who received glycine intravenously showed no objective improvement. This patient also failed to respond to glycine per os.

*Ephedrine*.—Ephedrine was administered to all the patients, but had no effect in relieving the symptoms in numbers 2, 3 and 4. The remaining three (cases 1, 5 and 6) experienced symptomatic improvement while taking the drug, but in only one (case 6) was the action apparently

\*We are indebted to the Connaught Laboratories for the supply of glycine used in this investigation, which was provided through the kindness of Dr. E. W. McHenry.

specific. It was clearly shown by repeated observations that ephedrine alleviated the severe symptoms in this case, and that withdrawal of the drug resulted in a rapid relapse into a state of profound myasthenia. It may be of significance that this patient obtained maximum benefit from an amount of ephedrine ( $1\frac{1}{2}$  gr. daily) which was not tolerated in other cases.

The other two patients (cases 1 and 5) obtained much less benefit from ephedrine alone. Some symptomatic improvement was noted, but no definite alleviation of symptoms was evident. Both these patients, unlike number 6, also received benefit from glycine, but showed maximal improvement when they were receiving both glycine and ephedrine. In both instances the best results were obtained by pushing the drug to the limits of tolerance. This contrasts with glycine therapy, in which larger doses appear to be no more beneficial than small ones.

*X-ray irradiation of the thymus gland.*—This method of treatment has been known for many years, but, despite encouraging reports of individual cases benefited by the treatment, it does not seem to have been used very extensively. In our small series of cases the results would appear to indicate that it has definite value in bringing about a remission. A course of treatment consisted of three irradiations with a dosage of 800 R. units each. These were applied to the mediastinum in the anterior, right and left posterior oblique positions.

Four patients were treated by this method (cases 1, 2, 3 and 4). In none of them was any enlargement of the thymus gland demonstrated clinically or by x-ray. Two showed marked improvement within a short time of receiving a course of treatment. Patient 3, with a two-year progressive history of symptoms, commenced to improve a few weeks after the first treatment and proceeded gradually to a complete remission. Patient 2, with a four-year history of myasthenic symptoms, commenced improving a few days after the last treatment and became symptom-free in two months. The remission in this case lasted two years before recurrence of symptoms. This second relapse was treated with glycine with equal success. In the other two cases treated by x-ray it is doubtful what part the treatment played in the improvement. Case 1 failed to show definite improvement until three months following the last treatment. At that time only a partial relief from symptoms occurred, which lasted six months. The progressive increase in symptoms over a period of three years prior to the administration of x-ray therapy is the only reason for assuming that the treatment may have been responsible for the improvement.

In Case 4 there had been a previous relapse of two weeks' duration from which spontaneous recovery occurred. Prior to receiving x-ray treatment symptoms had been present for six months. Improvement commenced six weeks after the last treatment and during the past nine months has slowly continued. The same doubt regarding the importance of x-ray therapy in effecting this improvement exists as in Case 1. In Cases 2 and 3 it seems probable that the remissions may have been started by this method of therapy. Despite the absence of any conclusive evidence, one feels that this treatment should be used more extensively than it has been in the past.

*Prostigmine.*—The four patients (cases 1, 4, 5 and 6) having symptoms of myasthenia gravis at the time the action of this drug was reported were each given an injection of prostigmine, 2.2 c.c., and atropine, 1/150 gr., subcutaneously. A marked temporary improvement in the power and resistance to fatigue of the affected muscles was noted in all cases. The improvement developed rapidly, reaching its maximum within an hour following the injections. However, the muscles gradually resumed their former state in a few hours and the myasthenic symptoms became usually slightly worse than they had been before the treatment was administered. On this dosage of prostigmine complete relief of symptoms was not obtained in any case. The muscles which were least benefited were those which had been weak for the longest time. Two patients (cases 1 and 5) received prostigmine on successive days. The beneficial effects were a little less marked with each succeeding injection, and the weakness and fatigability of the affected muscles became pro-

gressively worse after the effect of the drug had worn off, so that on the seventh and third days, respectively, it was considered unsafe to give any further injections to these patients.

*Physostigmine salicylate.*—Physostigmine salicylate, in doses varying from  $1/24$  gr. to  $1/6$  gr., with tincture of belladonna, 5 min. to 15 min., was administered to four patients (cases 1, 4, 5 and 6) without any beneficial effect. In all cases myasthenic symptoms actually became worse during the treatment and were usually associated with varying degrees of nausea and malaise. When glycine or ephedrine were substituted for physostigmine a rapid return to their former condition was noted in patients 1 and 6, suggesting that their relapses had been due to stopping these substances. One patient (case 5) showed definite improvement when glycine, 10 grams three times a day, was added to the treatment of physostigmine salicylate,  $1/6$  gr., and belladonna, 10 min., twice daily. However, this patient, unlike the others, had suffered no nausea or general symptoms as a result of the physostigmine.

*Antuitrin.*—Two patients (cases 1 and 5) received nine consecutive daily injections of 1 c.c. antuitrin intramuscularly. In neither case was any benefit obtained.

## DISCUSSION

Judging by the experience in this series of cases, the prognosis for life in myasthenia gravis would appear good when modern methods of treatment are employed. With the exception of Case 4 all the patients in this series were severely prostrated at some period of their illness, yet no fatalities have occurred to date. On the other hand, only 2 of the 6 patients have recovered sufficiently to permit return to full activity. Of the remaining patients, two are able to lead restricted lives with moderate comfort, but would only be capable of part-time duty. The other two are unable to do work of any kind.

In this small group of cases the results of treatment clearly indicate that great variation exists in the response of patients to the various remedies. This would suggest that the factors which determine the development of the symptom-complex known as myasthenia gravis may vary in different individuals. With the exception of antuitrin intramuscularly and physostigmine salicylate per os, which produced no definite improvement in the patients to whom they were administered, all the other forms of therapy were beneficial in certain cases. Of these latter, prostigmine subcutaneously gave the most consistent results, but the temporary nature of the improvement, the method of administration, and the cost all render it impracticable for continuous use. Further, it must be considered that the disturbed function of the muscles is not fundamentally altered by the administration of prostigmine. This is shown by the complete reversion of the affected muscles to their former state when the effect of the drug wears off. It has been suggested that the increased usage of

the muscles permitted during the temporary remissions may prove actually harmful if repeated too often. This was shown in two of our patients (cases 1 and 5) with severe generalized myasthenia. Daily administration of prostigmine had to be discontinued because of very pronounced weakness which developed five hours after the sixth injection in one case, and about the same time after the third injection in the other. It would seem that prostigmine subcutaneously is not likely to prove of much value in the therapy of this disease apart from its uses as an emergency measure in treatment and as a therapeutic test in diagnosis.

There still remain at our disposal three principal forms of therapy which appear to be of value in this disease; x-ray irradiation of the thymus gland, glycine, and ephedrine. The first of these may be effective in bringing about a remission. The latter two remedies, either together or separately, may give some measure of symptomatic relief. To decide which treatment will give the best results requires a process of trial and error. In evaluating the results of any remedy it is necessary to consider the tendency of the disease to spontaneous remissions and the frequent variation in the severity of the symptoms which may occur as a result of many factors, both intrinsic and extrinsic.

It was observed repeatedly in these patients that minor infections, emotional stress, hot baths, and mild gastrointestinal upsets were liable to produce marked increase in the fatigability and weakness of the affected muscles. In certain female patients a relapse is associated with each menstrual period (See case 1), whereas in other patients the severity of the symptoms bears no relation to the menstrual cycle (cases 3 and 6). Likewise, as pointed out by Laurent,<sup>12</sup> pregnancy in some patients may bring about a relapse, whereas in others a remission occurs while the patient is pregnant. In this connection, it is of interest that patient No. 3 has had two pregnancies in the past two years without a return of symptoms. There can be no doubt that exercise to the extent of fatigue aggravates the disease, particularly if continued over many days or weeks. These patients are always benefited by rest such as is obtained when they stop work. However, it is questionable whether complete rest in bed for long periods is of much value. In our experience, patients usually do better if they are allowed to take mild exercise short of fatigue.

#### SUMMARY AND CONCLUSIONS

1. Six cases of myasthenia gravis are reported, and their responses to different types of treatment are discussed in some detail.

2. Allowing for the tendency of the disease to spontaneous remissions and the frequent variation in the severity of the symptoms in the absence of treatment, the results in this series tend to confirm the view that x-ray irradiation of the thymus gland may be effective in some cases in bringing about a remission of months' or years' duration, and that glycine and ephedrine, either together or separately, are of value in obtaining symptomatic improvement in certain cases.

3. Glycine intravenously may produce symptomatic improvement in patients who respond to glycine per os, but it is apparently less effective. However, it might be useful as an emergency measure when a patient is unable to swallow.

4. The variability noted in the response of different patients to different remedies, particularly to glycine and ephedrine, is emphasized, and this suggests that the clinical syndrome of myasthenia gravis may be caused by different chemical factors.

5. Two methods of treatment which have been advocated failed to give any beneficial results in our experience, namely, physostigmine salicylate per os and antuitrin intramuscularly.

6. The dramatic effect of prostigmine, administered subcutaneously, in producing a temporary improvement was observed in four cases, but it is impracticable for continued use, and the fatigue subsequent to several consecutive injections may reach serious proportions.

7. The prognosis for life is good with modern methods of treatment, but it is only fair for complete remission of symptoms. Two of the cases in this series are in remission and the patients are carrying on at their regular activities. Two have improved to a degree where part-time occupation is possible. The remaining two patients, although somewhat improved by treatment, are totally incapacitated for any form of remunerative occupation.

I wish to express my thanks to Prof. Duncan Graham for permission to publish these case reports.

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## THE RADIOLOGICAL TREATMENT OF CANCER: METHODS AND RESULTS

1928 - 1935

### II. CARCINOMA CERVICIS UTERI\*

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FOR the past seven years an organized group representing the Departments of Gynaecology and of Radiology in the Toronto General Hospital has undertaken the joint study and treatment of a steadily increasing number of patients suffering from carcinoma of the uterine cervix. Following the organization of the Ontario Institute of Radiotherapy in 1934 the work has been carried on by the same group, thus enabling a report to be presented covering the entire period 1928 - 1935. During that time 227 public ward patients were treated with radium supplemented by high voltage x-ray. This series includes only those cases which had not received any active treatment previously, nor does it include cases in which the tumour involved the stump of cervix remaining after supra-vaginal hysterectomy performed at some previous date for a non-malignant condition. The comparatively small number of cases treated does not present a logical basis upon which to state percentage of cure rates. Nevertheless the follow-up has been very satisfactory, due in no small part to efficient social service and secretarial work.

### STATISTICAL TABLES

The Tables which follow present the survival of patients after treatment. Therefore the fact that three patients are reported as dying from extraneous disease does not affect the percentage survival rate, as they have been included in the report notwithstanding the fact that one died from tuberculosis and another from diabetes, although being apparently free from cancer. The other patient died from pulmonary embolism four days after treatment and has been specially noted, to draw attention to this one operative death.

Table I presents the survival Table of the whole series. The two five-year groups are very small. It is felt, however, that the one- and two-year survival groups present an interesting comparison, as the improvement under more complete and standardized treatment is evident. The analysis at the foot of the Table suggests that it may be anticipated that these same good results should carry through to the five-year period. At any rate the five-year period is no longer taken as the absolute criterion of cure, but has become rather a figure of speech. Over 40 per cent of the patients have been over fifty

\* The first article of this series appears in the September issue of this *Journal*.

years of age, and for them at least the mark of success may well be a symptom-free year.

#### CLINICAL CLASSIFICATION

The classification of Schmitz has been followed. The individual factor markedly affects any tabulations, and it is only after repeated examinations, vaginal, rectal and by speculum, that an accurate estimate of the extent of the disease may be determined. All extensive growths have an associated inflammatory reaction which not infrequently causes considerable cellulitis. In treated cases there often is scar-tissue formation in the recto-vaginal septum which may be very hard to differentiate except by repeated observations.

The extent of the disease is the basis for prognosis. Early diagnosis remains very difficult, as cancer of the cervix in its early phase is as silent as early malignant disease elsewhere. The symptoms commonly associated with its further development often cause the patient no alarm, or else fear keeps her from consulting a physician. The pitfalls which face the physician are many. Experience shows that a quarter of our patients have been under forty years of age and in many cases, in the absence of careful examination, the incipient growth had been treated by drugs, douches and local applications. Stage I carcinoma is rarely marked by well established symptoms, and must be diagnosed, often on a mere suspicion, by biopsy or diagnostic curettage.

It has been stated that post-operative cases have not been included in this review. The fact seems to be hard to establish that the eradication of cancer of the cervix by hysterectomy is an extremely difficult procedure, even in the hands of the most skilled, and yet a considerable number of patients have come to the Institute a few weeks after hysterectomy with the pelvis already filled by malignant involvement of the vaginal vault and cellular tissues. In several cases the cervix was *in situ* and the body of the uterus alone had been removed. The Tables show that there has been an increasing percentage of early cases coming to the clinic, and it is to be noted that when this was not the case, as in 1932, when only 40 per cent were stage I and II, as compared to 54 per cent in 1933, the results of treatment reflected this fact. Naturally, the main problem is the control of cancer, once invasion of the surrounding tissues has developed.

It is probable that the failure to cure many early cases is due to inability to determine the lymphatic spread. The value of high voltage x-ray as a supplement to radium is evident in the results from 1931 on to the present, and it was only last year (1935) that the fractionated method of Coutard was adopted as a routine. The results for that year speak for themselves, especially in advanced cancer, where often it was the only form of treatment. These years of observation have taught that the time is gone when a cure may be expected by a day or two of treatment. Just as the patient suffering from tuberculosis must face with fortitude

TABLE I.

#### CARCINOMA OF CERVIX UTERI: SURVIVAL TABLE BY YEARS CONTROLLED TO DECEMBER, 1935

GENERAL TABLE INCLUDING ALL CASES IN THIS REPORT: PERIOD 1929 TO 1935, INCLUSIVE

Year	Total	1 Yr.	Per-cent	2 Yrs.	Per-cent	5 Yrs.	Per-cent
1929	11	5	45.4	3	27.1	3	27.1
1930	18	10	55.5	7	38.8	5	27.7
1931	30	19	63.3	16	53.3		
1932	30	16	53.3	10	33.3		
1933	37	24	66.6	22	61.1		
1934	47	29	61.7				
1935	54	43	79.6				
Total	227						

Total of 227 cases of carcinoma cervix uteri were treated during the period 1929 to 1935.

Of these 134 are living and 104 are dead or untraced.

Of the 104 dead or untraced:

- 99 have died of cancer.
- 3 have died of extraneous disease.\*
- 2 are untraced.

Of the 123 living:

- 3 are living 6 yrs. of whom 3 are symptom-free.\*\*
- 5 are living 5 yrs. of whom 5 are symptom-free.
- 13 are living 4 yrs. of whom 13 are symptom-free.
- 8 are living 3 yrs. of whom 8 are symptom-free.
- 22 are living 2 yrs. of whom 19 are symptom-free;
- 3 are still under treatment.
- 29 are living 1 yr. of whom 23 are symptom-free;
- 6 are still under treatment.

80 are living 1 to 6 yrs. of whom 71 are symptom-free;  
9 are still under treatment.

43 are living less than 1 yr. of whom 18 are symptom-free; 25 are still under treatment.

123 living December, 1935, of whom 89 are symptom-free; 34 are still under treatment.  
Percentage of cases untraced, approximately 0.89%.

\*One of these patients died of pulmonary embolism four days after radium treatment.

\*\*The term symptom-free throughout this report is used to indicate that the patient is free from any evidence of the malignant disease for which treatment was undertaken as determined by the usual methods of clinical investigation.

tude months and years of care and supervision, so must the cancer patient. The concentration of a group of patients so controlled permits constant rechecking of results and so the evolution of more rational and thorough treatment.

#### RADIOLOGICAL METHODS

The analysis of the results of treatment as indicated in the Tables accompanying this paper was originally undertaken for the purpose of discovering to what extent the methods used in treatment might be considered satisfactory or if changes might be required. The conclusions reached may be indicated briefly, though space does not permit descriptions of technical procedures.

*Stage I.*—There were 34 cases altogether, of whom one patient was untraced and one had died of tuberculosis four years after treatment of her cancer without recurrence of the growth. There had been no deaths from cancer in this group in the 7-year period and of 32 living pa-

TABLE II.  
CARCINOMA OF CERVIX UTERI: STAGE I  
SURVIVAL TABLE BY YEARS  
CONTROLLED TO DECEMBER, 1935

*Key:*  
D.D.—Died of disease, *i.e.*, cancer.  
D.E.D.—Died of extraneous disease.  
Unt.—Untraced.

Year	No.	1 Yr.	2 Yrs.	3 Yrs.	4 Yrs.	5 Yrs.	6 Yrs.
1929	1	1		1	1		
1930	3	2	2	2	2	2	1
		1 unt.					
1931	5	5	5	5	4		
				1 D.E.D.			
1932	1	1	1	1			
1933	7	7	7				
1934	11	11					
1935	6	6					
Total	34						

Total of 34 cases of carcinoma of cervix uteri, stage I, were treated during the period 1929 to 1935. Of these 32 are living and 2 are dead or untraced December, 1935.

#### Of the 2 dead or untraced:

- 1 has died of extraneous disease (tuberculosis).
- 1 is untraced.

#### Of the 32 living:

- 1 is living 6 yrs. of whom 1 is symptom-free.
- 2 are living 5 yrs. of whom 2 are symptom-free.
- 4 are living 4 yrs. of whom 4 are symptom-free.
- 1 are living 3 yrs. of whom 1 is symptom-free.
- 7 are living 2 yrs. of whom 7 are symptom-free.
- 11 are living 1 yr. of whom 11 are symptom-free.

26 living 1 to 6 yrs. of whom 26 are symptom-free.  
6 living less than 1 yr. of whom 4 are symptom-free;  
2 are still under treatment.

32 living December, 1935; of whom 30 are symptom-free; 2 are still under treatment.

tients 30 were symptom-free. The two patients who could not be so considered had been treated within the year.

It was felt that the results in this group were very encouraging, and accordingly no drastic changes have been made in method. Patients in this group are treated primarily by radium. The dose used is 8,400 mg. hrs., using a filter equivalent to 1.5 mm. of platinum within the uterus and 2.5 mm. in the vaginal portion of the applicator. The chief point in carrying out the treatment is meticulous care in placing the radium, combined with the least possible handling and traumatism of the tissues.

TABLE III.  
CARCINOMA OF CERVIX UTERI: STAGE II.  
SURVIVAL TABLE BY YEARS  
CONTROLLED TO DECEMBER, 1935

Year	No.	1 Yr.	2 Yrs.	3 Yrs.	4 Yrs.	5 Yrs.	6 Yrs.
1929	4	3	1	1	1	1	1
1930	7	5	3	3	2	2	
		2 D.D.	2 D.D.		1 D.D.		
1931	10	7	6	6	6		
		2 D.D.	1 D.E.D.				
1932	11	11	8	6			
			3 D.D.	2 D.D.			
1933	13	12	10				
		1 D.D.	2 D.D.				
1934	19	12					
		7 D.D.					
1935	18	18					
Total	82						

Total of 82 cases of carcinoma cervix uteri, stage II, were treated during the period 1929 to 1935. Of these 55 are living and 27 are dead or untraced December, 1935.

#### Of the 27 dead or untraced:

- 25 have died of cancer.
- 1 has died of extraneous disease (diabetes).
- 1 is untraced.

#### Of the 55 living:

- 1 are living 6 yrs. of whom 1 is symptom-free.
- 2 are living 5 yrs. of whom 2 are symptom-free.
- 6 are living 4 yrs. of whom 6 are symptom-free.
- 6 are living 3 yrs. of whom 6 are symptom-free.
- 10 are living 2 yrs. of whom 9 are symptom-free.
- 10 are living 2 yrs. of whom 9 are symptom-free;
- 1 is still under treatment.
- 12 are living 1 yr. of whom 9 are symptom-free;
- 3 are still under treatment.

37 living 1 to 6 yrs. of whom 33 are symptom-free;  
4 are still under treatment.

18 living less than 1 yr. of whom 11 are symptom-free;  
7 are still under treatment.

Total of 55 living December, 1935, of whom 44 are symptom-free; 11 are still under treatment.

*Stage II.*—There were 82 cases in this group. Fifty-five are living while 26 are dead and 1 is untraced. Of the 55 living patients 44 are

symptom-free and 11 are still under treatment or are not free of disease. It is our conclusion that only the early cases in this group are suitable for radium as the primary method and that all the late stage II cases should be treated as recommended for the next group. The technical details of the radium treatment are much as for stage I.

*Stage III.*—The study of the results in this group was most instructive. Prior to the extended use of high voltage x-ray therapy, as will be seen by a reference to Table IV, the deaths in each year in the stage III cases were usually more than 50 per cent. This was accompanied by great difficulty in treatment, owing to massive tumours, secondary infection, etc., and the chief effort in treatment was to perfect ways and

means of dealing with this. Following the more thorough application of high voltage x-ray therapy (200 K.V.P.) there has been a decided improvement. In cases which respond favourably the massive tumours undergo recession, secondary infection disappears, ulceration heals, and the technique of the radium application is greatly simplified. Hence in all stage III cases treatment is commenced by a very thorough and protracted course with high voltage x-ray. It is very probable that *all* stage II cases and certainly *all late* cases in that group would be greatly benefited by being treated in a similar manner. The chief difficulties in carrying out such a procedure are economic and technical. Each treatment occupies from forty to sixty minutes, and in patients weighing more than 150 lbs. two such treatments per day are desirable. Such daily treatments (except Sunday) are continued for from four to six weeks. Following the completion of the x-ray series the radium treatment is carried out either immediately or after a short interval, depending upon the individual case. Comparing the figures for the year 1932 with those for 1935, there has been an improvement of about 26 per cent, almost all of which is due to the more thorough application of this method. To what extent this apparent improvement will influence future figures cannot of course be predicted, though it seems reasonable to expect a substantial increase in the percentage cure rate. If this should prove to be the case it will have a very important bearing on the manner of dealing with this disease. Technical methods in carrying it out permit of much greater refinement, which should add still further to benefits already obvious. For the present therefore the conclusion reached is that in all stage III cases and in some at least of stage II the primary method of treatment should be by the protracted fractional method of administering high voltage x-ray therapy and that this should as a rule precede rather than follow the use of radium.

*Stage IV.*—In common with others we have reached the conclusion that radium is seldom if ever indicated as the primary method of treatment during this stage. Accordingly treatment is commenced by high voltage x-ray and radium is used only in those few cases whose progress under this form of therapy reaches a point where its use is indicated. Cures are not expected, but

TABLE IV.

CARCINOMA OF CERVIX UTERI: STAGE III.  
SURVIVAL TABLE BY YEARS  
CONTROLLED TO DECEMBER, 1935

Year	No.	1 Yr.	2 Yrs.	3 Yrs.	4 Yrs.	5 Yrs.	6 Yrs.
1929	6	1	1	1	1	1	1
		5 D.D.					
1930	5	2	2	2	1	1	
		3 D.D.			1 D.D.		
1931	9	7	5	3	3		
		2 D.D.	2 D.D.	2 D.D.			
1932	11	4	1	1			
		7 D.D.	3 D.D.				
1933	9	4	4				
		4 D.D.					
1934	10	1 D.E.D.					
		5					
1935	19	14					
		5 D.D.					
Total	69						

Total of 69 of cases of carcinoma of cervix uteri, stage III, were treated during the period 1929 to 1935. Of these 29 are living and 40 are dead, December, 1935.

*Of the 40 dead:*

39 have died of cancer.  
1 has died of extraneous disease (post-operative embolism).

*Of the 29 living:*

1 is living 6 yrs. of whom 1 is symptom-free.  
1 is living 5 yrs. of whom 1 is symptom-free.  
3 are living 4 yrs. of whom 3 are symptom-free.  
1 is living 3 yrs. of whom 1 is symptom-free.  
4 are living 2 yrs. of whom 3 are symptom-free;  
1 is still under treatment.  
5 are living 1 yr. of whom 3 are symptom-free;  
2 are still under treatment.

15 living 1 to 6 yrs. of whom 12 are symptom-free;  
3 are still under treatment.  
14 living less than 1 yr. of whom 3 are symptom-free;  
11 are still under treatment.

Total of 29 living December, 1935, of whom 15 are symptom-free; 14 are still under treatment.

much palliation may sometimes be obtained as indicated by prolongation of life, and, perhaps

TABLE V.

**CARCINOMA OF CERVIX UTERI: STAGE IV.  
SURVIVAL TABLE BY YEARS  
CONTROLLED TO DECEMBER, 1935**

Year	No.	1 Yr.	2 Yrs.	3 Yrs.
1930	3	1	—	
1931	6	2 D.D.	1 D.D.	
1932	7	—		
1933	8	1	1	
1934	7	7 D.D.	—	
1935	11	5	6 D.D.	
Total..	42			

Total of 42 cases of carcinoma of cervix uteri, stage IV, were treated during the period 1929 to 1935. Of these 7 are living and 35 are dead, December, 1935.

*Of the 35 dead:*

35 have died of cancer.

*Of the 7 living:*

1 is living 2 yrs. and is still under treatment.  
1 is living 1 yr. and is still under treatment.  
5 are living less than 1 yr. and are still under treatment.

Total of 7 living December, 1935; of whom 7 are still under treatment.

more important than this, the added comfort which is derived from cessation of foul discharge and relief of pain. Even this is not constant and therefore every effort should be made by means of early diagnosis and prompt and efficient treatment to permit as few cases as possible to reach this stage. We know of no more effective way of adding emphasis to this observation than by inviting a comparison of the results of treatment in groups I and IV as recorded in the Tables which accompany this paper. It is scarcely necessary to draw attention to the obvious fact that all the cases in group IV were at one time in stage I, and had they been recognized and promptly treated at that period the prognosis for each would have been as favourable as it now is hopeless.

One of the greatest contributions which the medical profession can make towards this end would be to refer such cases as are being sent for treatment with as little preliminary interference as possible, except possibly a biopsy. Partial operations are worse than none at all and seriously jeopardize the prospect of successful radiotherapy. Since the latter clearly offers the patient more hope of cure than any other method at present available it should be carried out under as favourable conditions as possible.

## THE RADIOLOGICAL TREATMENT OF CANCER: METHODS AND RESULTS

1928 - 1935

### III. MALIGNANT LESIONS OF THE TONSIL AND ITS PILLARS

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THE clinical material upon which this study is based consists of 52 cases of malignant lesions involving the tonsil or its pillars, treated during the period 1928 - 1935, inclusive. Of these, 42 cases were carcinomata while 10 were sarcomata. Of the 42 patients diagnosed as having carcinoma 17 are living, of whom 15 are symptom-free\*; 2 have died of extraneous dis-

ease without recurrence of their malignant growth which had been controlled by treatment; 21 have died of cancer; and 2 are untraced. Of the 10 sarcoma patients, 5 are living and 5 are dead. The details in each group are as follows:

#### CARCINOMA OF THE TONSIL

A total of 42 cases were treated during the period 1928 to 1935. Of these 17 are living and 25 are dead or untraced, December, 1935.

*Of the 25 dead or untraced:*

21 have died of cancer.  
3 have died of extraneous disease.  
1 is untraced.

\* The term "symptom-free" is here used to indicate that the patient is free from any evidence of the malignant disease for which treatment was undertaken, as determined by the usual methods of clinical investigation.

*Of the 17 living:*

2 are living 7 yrs. of whom 2 are symptom-free.  
 1 is living 6 yrs. of whom 1 is symptom-free.  
 2 are living 3 yrs. of whom 2 are symptom-free.  
 2 are living 2 yrs. of whom 2 are symptom-free.  
 3 are living 1 yr. of whom 2 are symptom-free.

10 living 1 to 7 yrs. of whom 9 are symptom-free.  
 7 living 1 yr. or less of whom 6 are symptom-free.

Total of 17 living, December, 1935—40%  
 Of these 15 are symptom-free—35%  
 2 are still under observation.

**SARCOMA OF TONSIL**

Ten cases of sarcoma of tonsil were treated during the period 1928 to 1935. Of these 5 are living and 5 are dead.

*Of the 5 dead:*

All have died of sarcoma.

*Of the 5 living:*

1 has survived 6 yrs. and is symptom-free.  
 1 has survived 3 yrs. and is symptom-free.  
 1 has survived 2 yrs. and is symptom-free.  
 2 are living 1 yr. or less.

Total of 5 living December, 1935; of whom all are symptom-free. (All were lympho-sarcomata.)  
 All cases accounted for.

**PATHOLOGY**

The pathological classification has been simplified as much as possible, and according to this nomenclature the tumours fell into the following groups:

TABLE I.

Epidermoid carcinoma.....	28
Transitional cell carcinoma.....	5
Basal-cell carcinoma.....	2
Carcinoma, not specified.....	3
Lympho-sarcoma.....	5
Fibro-sarcoma.....	2
Hodgkin's sarcoma.....	1
Sarcoma, not specified.....	2
Biopsy negative.....	1
No biopsy recorded.....	3
	52

The patient in whom the biopsy was negative died within six months of cancer of the tonsil. Of those in whom no satisfactory biopsy was recorded, one was case No. 30-2, clinically very advanced, and is one of the untraced cases. A second was case No. 31-1, also advanced, and this patient died of mediastinal involvement two years after the treatment of his primary lesion. The third was case No. 29-2 who is still alive and symptom-free. His was a very typical case on clinical examination, and the diagnosis is undoubtedly accurate.

Table II shows the cases re-grouped according to the pathological findings and indicates the ultimate result in each group.

TABLE II.

	Total Cases	Living	Dead	Un-traced
Epidermoid carcinoma.....	28	10	17	1
Transitional cell carcinoma.....	5	3	2	
Basal-cell carcinoma.....	2	2	0	
Carcinoma, not specified.....	3	1	2	
Lympho-sarcoma.....	5	5	0	
Fibro-sarcoma.....	2	..	2	
Hodgkin's sarcoma.....	1	..	1	
Sarcoma, not specified.....	2	..	2	
Negative biopsy.....	1	..	1	
No biopsy.....	3	1	1	1
	52	22	28	2

Considering the question of success or failure therefore from the standpoint of the pathological findings alone, it would appear that the opinion generally held is correct, namely, that of the carcinomata the basal-cell type offers the most favourable prognosis, the transitional type the next most favourable, and the epidermoid type is the least favourable as well as the most common lesion.

In the sarcomata it will be noted that all the successful results were in the group of lympho-sarcomata, in which in fact there were no failures. While the number of cases is too small to give this observation a great deal of significance it does serve to emphasize the radiosensitivity of this type of tumour.

**ANALYSIS OF RESULTS**

Apart from reasons inherent in the pathological nature of the tumours themselves, success or failure may be influenced by a number of complex factors, such as the age of the patient, his general condition and willingness to co-operate, the duration and extent of the growth, etc. But, broadly, medical interest is centred on two questions mainly: to what extent was treatment successful in controlling (1) the primary lesion and (2) glandular secondaries, and in each case what part did radiotherapy play and what part was taken by surgery? To go into great detail in answering these questions is outside the scope of the present paper but much of the essential information may be condensed and is as follows:

**TREATMENT OF THE PRIMARY LESION**

*The carcinoma group*—42 cases.—In 39 of these radiotherapy was the sole method used in dealing with the primary lesion. Disappearance of the lesion and primary healing were obtained

in 32, while in 3 no opportunity of re-examination following treatment was afforded, so that accurate information on this point was not obtainable. In the remaining 4 cases the treatment failed to produce satisfactory healing. Chief interest therefore attaches to the 32 cases in which healing of the primary lesion was obtained. Of these 21 have remained healed without recurrence. Two additional cases healed and remained healed without recurrence until death ensued from other causes. Two others healed, then recurred locally, were again treated, and healed without subsequent recurrence. Thus in 25 of this group of 33 cases the primary lesion may be said to have been successfully controlled by radiotherapy. The other three cases of the series had previously been treated by surgical excision and were referred for post-operative prophylactic treatment. This was ineffective, as all three developed recurrences, either locally or elsewhere, and died of the disease. One of these patients might possibly have been saved by a surgical dissection of glandular secondaries but refused. It is our feeling that in this field if patients are to be referred for radiotherapy better results may be expected if no preliminary operation is undertaken, except in those cases in which the diagnosis has resulted from examination of material removed during simple tonsillectomy.

*The sarcoma group*—10 cases.—In two of these previous tonsillectomies had been performed and upon a study of the material removed the diagnosis had been made. In one case the disease involved both tonsils, and slides from both were positive. In this case recurrences were already present when treatment was undertaken, together with massive involvement of regional glands.

Of the 10 cases immediate healing of the primary lesion by radiotherapy was obtained in 8, one was treated post-operatively without the presence of a primary, and the tenth was a young child having an enormous primary in whom no satisfactory treatment was possible. None of the 9 cases in whom the primary lesion was controlled developed local recurrences, death being due in those cases whose treatment was finally unsuccessful to other factors (remote metastases 3 cases, failure to control glands, 1 case).

#### THE TREATMENT OF GLANDULAR SECONDARIES

This is a more complex problem. Of the 42 cases of carcinoma 14 presented no evidence of glandular secondaries on admission. In 11 of these no glands ever developed while three developed glandular secondaries at a later date. Twenty-eight patients had enlarged glands on admission. These were classified in three categories: (a) small, discrete glands, few in number, operable, 11 cases; (b) numerous, larger but not matted, operable, 12 cases; (c) massive involvement, inoperable, 5 cases; total 28 cases. One of the latter also presented extensive involvement of the mandible. All of the last group would be regarded as hopeless cases, and treatment was undertaken largely as a palliative measure.

The principle underlying the treatment of glandular secondaries in dealing with the cases here reported has been to operate upon all cases considered operable by the surgical consultant, but where possible this procedure has been postponed until after the treatment of the primary lesion has been completed, since, unless this lesion can be successfully controlled by radiotherapy, the patient should not be submitted to a major surgical procedure. This interval also provides an opportunity of carrying out a course of pre-operative irradiation of the glandular areas. If the glands disappear following this radiotherapy no operative procedure is undertaken, and "routine" dissections of the neck in the absence of palpable glandular involvement have not been done. The whole question of what is considered the proper method of dealing with the problem of glands will be more fully discussed in a later paper. For the present the facts are as follows.

1. *Cases without glandular involvement on admission.*—As has previously been stated there were 14 such cases and of these only 3 later developed glands. The extent to which this affects the final outcome is instructive. Of the 11 in whom no glands ever developed 6 are living and symptom-free; 2 additional patients died of intercurrent disease without recurrence, making 8 of the 11 cases which may be considered as having had a successful result from treatment, a much higher percentage than in the group having glandular complications as will be seen presently.

Cases in whom no glands developed—11.  
Living and symptom-free—6.

1 has survived 7 years.  
1 has survived 6 years.  
2 have survived 2 years.  
2 have survived 18 months.

Cases who have died—5.

Cases who have died of intercurrent disease—2.

1 pneumonia, without recurrence, after 3 yrs.

1 intestinal haemorrhage without recurrence, after 1 year.

Cases who have died of cancer—3.

1 extension of primary after 2 years.

1 extension of primary after 4 years.

1 pulmonary metastases after 6 years.

Of the three in whom glands developed later, the final result was as follows:

I. Case No. 28-1. Epidermoid carcinoma, right tonsil. Primary treated by radiotherapy 1928—no recurrence. Developed glands in right side of neck, 1933. Successfully treated by block dissection. No recurrence to date.

II. Case No. 30-1. Epidermoid carcinoma, left tonsil. Primary treated by radiotherapy 1930—no recurrence. Developed glands left neck five months later. These were treated by block dissection—no recurrence. Patient died of metastases in the liver 2 years later without recurrence of either the primary or the secondary.

III. Case No. 32-1. Epidermoid carcinoma, left tonsil. Referred for treatment following operative removal of primary together with dissection of neck. Four months later recurrence developed in the neck in spite of prophylactic irradiation and resisted all subsequent measures. Finally the primary also recurred and patient died within the year of extension of both.

Thus it may be said that in two of these cases surgery was the effective measure in dealing with the glandular problem, while in one case both surgery and radiotherapy failed.

2. *Cases having glandular involvement on admission: total 28.*—Class "A"—11 cases: 7 of the 11 cases in this group were treated by surgical dissection, sometimes combined with radiotherapy, either pre-operative, post-operative or interstitial. Of these, 5 remained free from recurrences in the neck and 3 are still symptom-free. Of the others, 1 case died of recurrence in the neck while the primary remained healed; 2 died of recurrences and extension of the primary only, the neck remaining healed; 1 died of recurrence of both primary and secondary. The details of the above information follow in Table III.

Class "B"—12 cases: 3 of the 12 patients were treated surgically, of whom 2 remain alive and free from recurrence, while one died of extension of the primary without recurrence in the neck. Two other patients in this group refused dissection of the glands, one at least of whom could very probably have been saved by this procedure. Nine were treated by radiological methods only. In 4 of these 9 cases the treat-

TABLE III.  
CLASS "A"

1 age 87	Primary only treated. Patient did not return.	Untraced.
1 " 58	Epidermoid carcinoma. Block dissection, bilateral. No post-operative radiation. Recurrence of primary.	Died of disease 1 yr. 2 mos.
1 " 72	Epidermoid carcinoma. Block dissection right side. No post-operative radiation. Recurrence in neck. No recurrence of primary.	Died of disease 6 mos.
1 " 58	Carcinoma. Block dissection right side. Post-operative radiation ineffective. Recurrence both.	Died of disease 2 yrs.
1 " 70	Epidermoid carcinoma. Block dissection left side; interstitial radiation and post-operative radiation. No recurrence.	Alive and well 3 yrs.
1 " 54	Epidermoid carcinoma. Block dissection left side; post-operative radiation. No recurrence.	Alive and well 3 yrs.
1 " 82	Primary only treated. Patient did not return.	Died of disease 6 mos.
1 " 77	Epidermoid carcinoma. Block dissection right side. No post-operative radiation. Recurrence of primary; no recurrence in neck.	Died of disease 9 mos.
1 " 60	Negative biopsy. Primary only treated. Patient did not return. Extension of primary.	Died of disease 6 mos.
1 " 63	Transitional cell carcinoma. External radiation only to neck, ineffective. Refused dissection. Extension to neck and mediastinum.	Died of disease 1 yr.
1 " 52	Basal cell carcinoma. Teleradium to glands ineffective. Block dissection left side. No recurrence.	Alive 1 yr.

Total, 11 cases.

ment has been successful in causing the entire disappearance of the glandular involvement and these patients remain symptom-free. One additional patient is classified as still under observation, while in one other the treatment was successful in controlling both the primary and secondary, but the patient died of mediastinal secondaries without returning for treatment of this complication. The details follow in Table IV.

Class "C"—5 cases: as will be obvious, all of the cases in this group were so advanced as to be hopeless of cure, only one patient was treated surgically, and in all cases the measure adopted was looked upon as palliative. The details follow in Table V.

*Summary regarding rôle of surgery*—A total of 14 cases were treated by surgical dissection, of whom 6 patients are living and 8 are dead. Ten of the number operated upon did not develop

TABLE IV.  
CLASS "B"

1 age 61	No biopsy. Both primary and glands treated radiologically. Both controlled. Mediastinal involvement developed and was not treated.	Died of disease 2 yrs.
1 " 62	Epidermoid carcinoma. Radiation only. Refused dissection. Extension of both primary and secondary.	Died of disease 1 yr.
1 " 52	Transitional cell carcinoma. Block dissection left side. Interstitial radiation. No recurrence.	Alive and well 3 yrs.
1 " 73	Epidermoid carcinoma. Block dissection right side. Extension of primary.	Died of disease 9 mos.
1 " 58	Transitional cell carcinoma. Block dissection right side. No recurrence.	Alive and well 2 yrs.
1 " 51	Transitional cell carcinoma. Radiation only. Refused dissection. Extension glands.	Died of disease 1 yr.
1 " 57	Epidermoid carcinoma. Radiation only treatment. Glands controlled by teleradium.	Alive and well 2 yrs.
1 " 60	Epidermoid carcinoma. Radiation only treatment. Glands controlled by teleradium.	Alive and well 2 yrs.
1 " 67	Epidermoid carcinoma. Radiation only treatment. Ineffective. Palliation only. Extension both.	Died of disease 6 mos.
1 " 62	Epidermoid carcinoma. Radiation only treatment. Refused dissection. Under observation.	Living 18 mos.
1 " 76	Carcinoma. Radiation only treatment. Glands disappeared (teleradium).	Alive and well 18 mos.
1 " 54	Transitional cell carcinoma. Radiation only treatment (teleradium). Glands disappeared. (Also primary Ca. Breast controlled by same method.)	Alive and well 18 mos.

Total, 12 cases.

recurrences in the site of operation while in four recurrences took place. The interpretation of these facts is complicated by the added fact that 12 of the cases were also treated radiologically either before or after the operative procedure, sometimes both.

#### *Summary regarding rôle of radiology.—*

##### 1. As a means of prophylaxis.

So many variable factors enter into the question of assessing the value of radiotherapy under these conditions as to make an accurate opinion extremely difficult to reach. In the present case one wishes to know, for example, to what extent radiation was responsible for preventing the development of glandular secondaries in those patients having no glands on admission. Eleven of the 14 received radiotherapy, 3 did not. Of

the latter one is alive and well six years later, no glands having developed. The only treatment was the radiological treatment of his primary. The second case developed glands and was successfully treated surgically. He is still symptom-free. The third died of recurrence of the primary after four years without glandular involvement at any time.

Eleven patients received radiotherapy. In 9 of these no glands developed, while glandular involvement later developed in two. In these two the radiological treatment was obviously ineffective as a prophylactic measure. How are the others to be interpreted? For the present no opinion is offered on this subject, though it is felt that 9 out of 11 is a rather high percentage to remain free from glandular complications, and suggests that there probably was some prophylactic value in this use of radiotherapy.

##### 2. As a means of treatment of existing glands.

Twelve of the 21 patients comprising groups "A" and "B" in whom palpable glands were present were treated solely by radiotherapy. In 7 of these the glandular masses disappeared and have not recurred to date. Five of these cases were in group "B" and two in "A". In four cases in each group this method was ineffective and surgical dissection became necessary. While therefore it is evident that radiotherapy is capable of causing the disappearance of glandular masses such results are neither uniform nor certain, and there is no suggestion that the method should replace surgery, but it should be used as an alternative in some cases.

TABLE V.  
CLASS "C"

1 age 88	Epidermoid carcinoma. Primary healed. Secondaries treated by radiation only. Ineffective. Extension of glands.	Died of disease 1 yr.
1 " 61	Epidermoid carcinoma. Block dissection. Resection mandible. Died of extension of primary and recurrence in neck.	Died of disease 6 mos.
1 " 59	Epidermoid carcinoma. Radiation only. Metastases in ribs and spine.	Died of disease 6 mos.
1 " 76	Epidermoid carcinoma. Radiation only. Not completed.	Died of disease 2 weeks.
1 " 70	Epidermoid carcinoma. Radiation only. Did not return (primary only treated).	Cannot trace.

Total 5 cases

The objection will of course be raised that there is no proof the glands which disappeared following radiotherapy were malignant, and since this is a controversy which cannot be settled, it is merely pointed out that in this paper when referred to as having so disappeared they have not been described as "secondaries" but merely as palpable glands. The important fact is that palpable glandular masses, in one case quite large masses were present and verified by more than one observer, and these masses have disappeared and have not recurred.

#### RADIOLOGICAL METHODS

In the treatment of malignant lesions of the tonsil we have been so favourably impressed by the improvement in results since full use has been made of teleradiumtherapy (*i.e.*, the 4 gramme radium bomb) that this method has now supplanted all others as the preliminary step in treatment. While making due allowance for the fact that our series of cases is small in any one year, yet it is apparent that in this disease the radium bomb finds one of its most successful fields of usefulness. During the year 1935 seven cases of carcinoma of the tonsil were treated by this means of whom 6 were entirely symptom-free at the end of the year, and the seventh became so later. No comparable results

have been obtained by us by methods previously available, and while it is not suggested that these patients are cured the record indicates a striking improvement in the therapy of this type of lesion.

As a result of this experience the method at present in use is as follows: The initial treatment consists of a carefully planned course of teleradium therapy, which includes the primary lesion and the entire area of regional lymphatics and is pushed to the point of a satisfactory tissue reaction, both in the tonsillar region and on the skin. In the majority of cases the primary lesion heals with no visible scarring. If it fails to do so, radium is applied locally by the interstitial method, using highly filtered needles.

In cases without glandular involvement, and in cases in which palpable glands are present and disappear following the treatment previously described, no surgery is undertaken. Such cases are kept under careful periodic observation and the treatment repeated as a prophylactic precaution. If, however, glands are present and fail to disappear following the first course of teleradium therapy, dissection of the neck is recommended, providing the primary lesion has been controlled or is responding favourably. The neck dissection in turn is followed by an intensive post-operative radiotherapy as the skin will tolerate without undue reaction.

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#### BASAL ANÆSTHESIA IN CHILDREN'S SURGERY\*

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**B**ASAL anaesthesia may be considered for the purpose of this discussion as a state of unconsciousness of such degree that the patient is unaware of the events incident to his removal from his bed to the operating room and to the administration of the supplemental anaesthetic. This also implies such a degree of amnesia that there is no subsequent memory of the operation. To illustrate with a concrete instance. An interval appendectomy was performed upon a seven year old child under basal anaesthesia. When an enema was given on the fifth post-

operative day he remarked, "I know what this is. They did it to me a while ago, and I think I had an operation." The contrast between that reaction and the usual post-operative memories is striking.

Undoubtedly some of the most indelible of the unpleasant impressions of childhood are those associated with an inhalation anaesthetic, and the resultant psychic shock may well bear a causal relationship to psychological maladjustments in later life. Dogmatic statements regarding mental reactions in children, as a class, are unwise in view of the diversity of types encountered. Children may be bold or timid, trustful and confiding, or suspicious, sensitive or phlegmatic, and each type will react differently

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to environment and to stimuli. A study of such reactions does not lend itself to methods of fixed physical measurements or accurately controlled factors, but certain observations are sufficiently common to be of significance.

A study of post-operative conditions at the Children's Orthopaedic Hospital revealed a definite correlation between post-operative acidosis and pre-operative emotional disturbance, the index of acidosis being the degree of acetonuria. Those children who approached operation in a calm, unfrightened state usually had minimum post-operative morbidity and little if any acetonuria, whereas those who were markedly disturbed pre-operatively usually had a stormy recovery with a high degree of acetonuria of two or more days' duration. In observations of this nature it is important to differentiate between the child who is actually unafraid and the one who is outwardly calm but inwardly terror-stricken. While the character of the operative procedure was no doubt a factor the intensity of emotional upset was found to have a much more direct influence. Acetonuria may be interpreted as evidence of increased metabolic activity with protein destruction and depletion of reserve, and is associated with increased activity of the autonomic nervous system and the endocrine glands. These physical reactions are manifest by physical signs.

What may be said of the psychic reactions? Gwathmey<sup>1</sup> has observed the development of stuttering in one child and the necessity of prolonged psychiatric care in another as a consequence of pre-operative fear and lack of sedation. Beverly,<sup>2</sup> in an excellent recent article, draws a striking picture of the all too prevalent lack of attention to the pre-operative environment of a child. In substance he says that the child is brought to the hospital with false assurances and persistent prevarication; his eyes, ears and nose are assailed by strange and usually disagreeable stimuli; impersonal and uninterested attendants separate him from the parents upon whom he has always relied for protection and security; he sees instruments which his little playmates may have fiendishly described as being used to cut off arms, legs and even heads; and, finally, he is held down on a table by the superior brute force of two or three adults while he passes screaming and struggling into suffocating unconsciousness. No child ever undergoes such an experience without being thoroughly frightened, and it is impossible to estimate the psychic damage and

sequelæ. One of the characteristics of human memory is that it is mercifully short for unpleasant experiences, but such an ordeal may well be a factor in a subconscious distrust of parents, favouring domestic maladjustments, or a fear of doctors and hospitals which may later delay medical consultation at a critical time, or influence a decision to turn to cultists.

The general surgeon, 80 to 95 per cent of whose patients are adults, is necessarily concerned with the problems of adult surgery. His initiative, ingenuity and time are quite properly directed primarily toward solving these problems rather than those of children's anaesthesia, which he usually considers of minor importance, the anaesthetic merely representing a more or less irritating delay to the primary incision. Anaesthetists, paediatric nurses, and those of us who are constantly confronted with the problems of infancy and childhood, however, have long been keenly aware of the inadequacy and defects of anaesthesia as usually employed in children's surgery, of the undesirable aspects of post-operative recovery, and of the unwholesome mental distortions and deviations which often result. Given a skilful, tactful anaesthetist, a child who has not been ruined by a previous badly administered anaesthetic and a surgeon who is not over-anxious to conserve a few minutes of his time, it is possible in practically all instances to induce satisfactory anaesthesia with any suitable inhalation anaesthetic agent. How rarely, however, do we meet such a happy combination! And how often is one of the major results of an operation the development of another anaesthephobe!

Pre-anaesthetic medication was developed to combat pre-operative difficulties, and it has been carried to a high degree of perfection, particularly for those adults whose nerves are irritated by toxins, or whose mental reactions are so disturbed as to render appeal to reason difficult. Strangely enough, in childhood when the nervous mechanism is being constantly bombarded by showers of strange impulses, and mental reactions are so undeveloped as to render appeal to reason impossible, pre-anaesthetic sedation was at first little used and even considered contraindicated.

With the development of the intravenous administration of barbiturates the long-awaited ideal anaesthetic for children seemed to have arrived, but again there was delay because the manufacturers could supply no information as to the dosage for children, and the earlier clinical

reports warned against its employment in the two extremes of life. The reason for such a warning was evidently fear of possible unfavourable reactions or unfamiliarity with children rather than actual observation of untoward results, as more extensive use has since proven. Now the child may remain quietly in bed talking normally with his parents and experience only the slight inconvenience of a needle puncture or an enema, with either of which procedures he is probably already familiar. Not until he has passed easily and quickly into a deep, quiet slumber is he moved to the operating room. The mental shock of parental separation and the physical shock of restraint and semi-asphyxia are entirely eliminated. Let me call it to your attention also that the psychological effect upon the parent is a most happy concomitant of this method of anaesthesia, as any one of us can well attest who has stood by while his own child has taken even the most skilfully administered inhalation anaesthetic.

Basal anaesthesia or narcosis may be induced by the various barbiturates administered by mouth, by vein, or by rectum; or by tribromethanol (avertin) or paraldehyde administered rectally. They have been termed irreversible anaesthetics, and have been considered uncontrollable because absorption can not be halted at any desired point as with the inhalation anaesthetics. This undesirable feature has been obviated to a great extent in the more recently developed forms which after absorption are rapidly broken down and excreted as non-toxic substances. An over dosage sufficient to cause depression and inhibition of respiration does not affect the heart, and thus it is possible to use respiratory stimulation or artificial respiration effectively during the comparatively short period required for excretion of the excess anaesthetic. Coramine intravenously is a most effective antidote. If an idiosyncrasy to barbiturates is suspected a small test dose may be given by mouth a day or two previous to the operation.

The rectal anaesthetics possess the advantage of employing a familiar procedure and not requiring a needle puncture with the occasional difficulty of entering a small or obscure vein. They are time-consuming, however, as they must be given slowly and should be started 20 to 30 minutes before the child is to go to the operating room. Where time of induction is a factor the quickly acting intravenous anaesthetics are to be preferred. Post-anaesthetic excitement

occurs more frequently after the barbiturates than after avertin or paraldehyde, but it is of short duration and easily controlled by morphine.

It has been stated that basal anaesthesia is contraindicated in operations on the upper respiratory tract, but Gwathmey reports that in tonsillectomies the safety factor is increased by adequate pre-anaesthetic medication, followed by a proper anaesthetic sequence.

Deaths have been reported following the use of avertin (Brown, Maddox), but under careful analysis they are found either to have occurred early in the development of these agents, or to have been due to faulty technique. They have generally followed the attempt to produce total instead of basal anaesthesia. Maddox<sup>3</sup> estimated that avertin had been used 1½ million times up to the date of his survey over two years ago, and the reported fatalities have been very few.

Medical literature of the past few years has contained a considerable number of references to intravenous and rectal anaesthesia, both basal and total, and many of these mention briefly that they are also of value in children. Recently, however, reports have begun to appear dealing entirely with the use of these agents in children, and the early vague fears and theoretical objections are disappearing. The profession in the United States seems to be slow to give up pre-medication by morphine, which does not eliminate psychic disturbance, and also rather tardy in following the lead of the British as regards basal anaesthesia in children. The demand for its use will no doubt come from the paediatricians and paediatric nurses rather than from the surgeons.

The intravenous barbiturates most frequently used at present are sodium amytal, pentothal, and evipal. They are quickly-acting, and the latter two are especially rapidly excreted. They occasionally cause post-operative restlessness and excitement, but nausea and vomiting are markedly reduced. Paraldehyde has been used rather extensively in Great Britain, but avertin is generally preferred for rectal administration. The barbiturates are also well tolerated and absorbed by the rectal mucosa, and may be used in this manner with excellent results.

Basal anaesthesia is contraindicated in toxic and cachectic children, and rectal administration should not be used in the presence of rectal or colonic inflammation. Healthy infants and young children tolerate full doses for their weight as well as older children and adults, the reason being, no doubt, that the younger the child, the

more active are the physiological processes, and hence the more rapid the elimination of the anaesthetic.

Personal experience with basal anaesthesia in infants and children, extending over more than four years, has been highly satisfactory, the only adverse observations being those already mentioned. The mental reaction of children who have been subjected to multiple operations and who have had the opportunity to make comparisons has been uniformly and enthusiastically favourable. They make little or no complaint of the discomforts or restraint incident to the operation, but are most vigorous in their protests against inhalation anaesthesia. The following remarks are typical: "I don't mind an operation, but I hate that ether"; "Please let me have that needle anaesthetic"; "If I have to come back may I have my anaesthetic by an enema again?" "I don't care how many operations I have if I may have that kind of an anaesthetic"; and so on.

The use of the barbiturates has been followed by post-anæsthetic excitement in about 10 per cent of our cases but this has always been easily controlled. There has been respiratory depression of varying degrees associated with the use of avertin, but only once to an extent requiring stimulation, the cause in that instance being too rapid administration. There have been no deaths and no occasions for anxiety other than the very temporary one just mentioned.

Details of physiological action and of administration are important but have been purposely omitted as coming more properly within the scope of a technical paper.

Basal anaesthesia should not supplant all other forms of pre-anæsthetic medication, nor is it suitable for all cases, for anaesthesia to be best must be individualized. It is, however, ideal for the great majority of cases in the field of surgical paediatrics. Children have for many years not only survived the usual types of anaesthetics but have grown to be healthy adults, and, no doubt, will continue to do so, due to their wonderful ability to adjust themselves to adverse conditions, but should we make this characteristic an excuse for giving them anything less than the best?

Let me urge upon you in behalf of all children who may in the future come to the operating table that you do your part in developing the popularity of this humane procedure by requesting basal anaesthesia whenever it is not definitely contraindicated. The paediatrician must lead the way. Both his clientèle and the profession at large will appreciate his tactful insistence upon thoughtful consideration of his little patients in a matter which so definitely affects not only their present physical comfort but also their future psychic development. Someone has well said "Anaesthesia is not a courtesy, it is a right". Permit me in closing to adapt that quotation to the present subject by saying that basal anaesthesia for children is not a courtesy; it is their right.

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**LIPOIDOSIS CUTIS ET MUCOSÆ.**—According to R. N. Tripp this disease was discovered independently by Wiethé in 1924 and Urbach in 1929, and its study was placed on a firm base by their joint investigation of nine cases in four families. In these cases, as well as a tenth described by Tripp, there were scattered deposits in the skin and mucous membranes of a lipoid, soluble in hot alcohol or acetone, and apparently a phosphatic lipoid closely related to, if not identical with, lecithin. Clinically the most prominent feature was hoarseness, due to laryngeal lipoidosis, appearing in the second year of life

at the latest; a familial incidence was well established. On the skin white nodular masses and hyperkeratotic lesions were present, on the face and proximal interphalangeal finger-joints in all cases. Infiltrations were common on and in the tongue and epiglottis. The condition, which is allied to xanthoma and necrobiosis lipoidica diabetorum, improves if treated with restricted carbohydrate intake and small doses of insulin. In several patients biochemical tests have shown a latent diabetic tendency.—*New York State J. of Med.*, April 15, 1936, p. 619. Abs. in *Brit. M. J.*

## PREGNANCY COMPLICATED BY RHEUMATIC HEART DISEASE\*

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PREGNANCY complicated by heart disease is a grave condition for both mother and child. The maternal mortality is high and premature birth is frequent. In our experience at the Toronto General Hospital the maternal mortality has varied, in previously reported cases, from 8.4 to 2.3 per cent. Eastman<sup>1</sup> estimates the maternal mortality at 8 to 5 per cent, and states that on that basis 1,000 women die annually in the United States from heart disease complicating pregnancy. An even more dramatic emphasis of the seriousness of this complication of pregnancy is made by Hamilton and Kellogg,<sup>2</sup> who state that 20 per cent of the maternal deaths at the Boston Lying-In Hospital over a period of four years were due to heart disease. W. Schuman<sup>3</sup> states that the second highest cause of maternal mortality at the Sinai Hospital, Baltimore is cardiac disease.

In 1933 the writer in conjunction with Prof. W. A. Scott<sup>4</sup> reported on a series of patients suffering from rheumatic heart disease and pregnancy delivered at the Toronto General Hospital. The problem of myocardial disease and pregnancy was considered in various aspects and certain general conclusions were drawn. Two of the conclusions resulted in broad changes of policy at our clinic in regard to the observation and management of the pregnant patient with heart disease. The first led to the establishment of a combined prenatal and cardiac clinic which has permitted personal consultations between cardiologist and obstetrician and a continuity of observation of all heart cases by one obstetrician and cardiologist. As far as practicable all labours are conducted by the same obstetrician. The second conclusion led to a radical change in the methods of delivery. In the series reported in 1933 Caesarean section was the method of delivery in 46.3 per cent of the cases. We concluded that this high incidence of Caesarean section was unwarranted and should be reduced.

The purpose of this paper is to give our present opinions in regard to heart disease and pregnancy,

and to report a new series of 35 deliveries. Included also, is a report of 11 pregnancies terminated because of rheumatic heart disease.

During the past three years 35 patients suffering from rheumatic heart disease and pregnancy have attended the combined prenatal cardiac clinic at the Toronto General Hospital. These patients have been divided into three groups according to the severity of their heart disease and are very similar in comparison to the cases previously reported in 1933. Table I presents

TABLE I.  
SEVERITY OF THE HEART DISEASE

	Previous Series 41 Cases Primiparae 15 Multiparae 26	Present Series 35 Cases Primiparae 15 Multiparae 20
Slight or no impairment of exercise tolerance...	16 cases	15 cases
Moderate to severe impairment of exercise tolerance.....	16 cases	14 cases
Failure.....	9 cases	6 cases
Total.....	41 cases	35 cases

such a grouping and comparison of the two series. Group 1 includes those patients with no or only slight impairment of exercise tolerance. Group 2 includes those with moderate to severe impairment of exercise tolerance, and Group 3 includes those who had cardiac failure. The patients were classified after delivery and many who would have been in Group 1 early in pregnancy were finally classified in Group 2. All patients who developed failure did so after the fourth month.

The methods of delivery for the two series of cases are shown in Table II. The incidence of spontaneous births is practically the same for

TABLE II.  
METHOD OF DELIVERY

Type of Delivery	Previous Series 41 Cases	Present Series 35 Cases
Spontaneous.....	39.0% (16 cases)	45.7% (16 cases)
Forceps.....	14.6% ( 6 cases)	51.5% (18 cases)
Cæsarean section and sterilization..	46.3% (19 cases)	2.8% ( 1 case)

\*From the Department of Obstetrics and Gynaecology, University of Toronto.

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both series. The great difference occurs in the incidence of forceps deliveries and Cæsarean section. Forceps were employed nearly four and a half times as frequently in the second group as in the first, while the incidence of Cæsarean section was reduced from 46 to 2.8 per cent. Both series of cases are small, nevertheless they show that practically identical results were obtained in similar cases by conservative as compared with radical methods of delivery. It seems reasonable to suppose that the constant employment of a serious abdominal operation in a larger number of cases would lead to a higher mortality than would simple forceps delivery.

There was one death from heart failure in both series. In the first series the death occurred twenty-four hours after a forceps delivery, while in the second series the death occurred twenty-seven days after induced labour and spontaneous delivery.

The complications of labour are shown in Table III. Premature birth occurred 7 times,

TABLE III.  
COMPLICATIONS OF LABOUR

<i>Complication</i>	<i>No. of Cases</i>	<i>Primiparæ</i>	<i>Multiparæ</i>
Premature births.....	7	3	4
Post-partum haemorrhage	1	0	1
Excessive post-partum bleeding.....	4	2	2

Average duration of labour in primiparæ, 18 hours.

or in 20 per cent of the cases, which is characteristic of pregnancy complicated by heart disease. The constant danger of post-partum haemorrhage in the cardiac patient is emphasized by one case of severe post-partum haemorrhage and 4 cases of excessive post-partum bleeding. The average duration of the first stage of labour in primiparæ, 18 hours, is mentioned as it is usually stated that labour is rapid in the patient suffering from heart disease.

In our experience over 90 per cent of heart disease complicating pregnancy is rheumatic in origin. The most common valvular lesions are mitral stenosis and insufficiency, although aortic insufficiency is not unusual. The diagnosis of heart disease and the estimation of the ability of the heart to stand the added strain of pregnancy are both frequently difficult. The large hypertrophied breasts of pregnancy interfere with the percussion of the heart borders, and the raised diaphragm, which occurs fairly early in

pregnancy, results in the rotation of the apex of the heart outwards, further adding to the difficulty of estimating the degree of cardiac hypertrophy. The murmurs also frequently change as the pregnancy progresses. It is not unusual to find at one examination a definite mitral diastolic murmur, only to discover that it has disappeared when the patient is next examined. Shortness of breath and dependent oedema, common symptoms of heart disease, are frequent accompaniments of normal pregnancy, particularly during the later months. These difficulties of diagnosis are all minimized in the early months of pregnancy, and are further evidence of the value of early prenatal examination and observation.

More than usual care should be taken in the routine heart examination of the pregnant patient or many cases of heart disease will be missed. A large percentage of patients suffering from this complication of pregnancy have no symptoms of heart disease (15 out of 35 in the present series), and hence nothing to direct attention to careful examination of the heart. An enquiry in regard to past attacks of rheumatic fever or chorea should be a routine question, and when such a history is elicited particular care should be exercised in the examination of the heart.

The progressive nature of rheumatic heart disease warrants particular emphasis when considered in relationship to pregnancy. A patient, 20 years of age, suffering from rheumatic heart disease may withstand the strain of pregnancy and labour without cardiac embarrassment, yet a few years later pregnancy may result in failure and death. In other words, the history of uneventful past pregnancies is no indication that a subsequent pregnancy will not cause a cardiac breakdown. In a previously reported series of 10 patients<sup>4</sup> who developed failure during pregnancy, 7 were multiparæ who had experienced relatively normal pregnancies up to the one causing the cardiac breakdown.

#### MANAGEMENT OF THE PREGNANT PATIENT WITH HEART DISEASE

The management of the pregnant patient suffering from heart disease can be conveniently discussed under three headings:—The management during the prenatal period, during labour, and during the puerperium.

*Management during the prenatal period.*—The first requisite here is frequent observation. The value of such prenatal examination is particu-

larly well emphasized by Lamb<sup>5</sup>, who reports a 2.2 per cent mortality where adequate prenatal care was carried out, compared with a 20 per cent mortality in patients who did not receive prenatal observation. The observation must be frequent. Our procedure is to have the patient visit the clinic twice a month until the eighth month, and each week from then on. We advise admission to hospital seven to ten days before the expected date of confinement for rest and observation. The reason for such frequent observation is to discover early cases that are developing progressive impairment of exercise tolerance or impending failure. Once cardiac insufficiency has occurred, the maternal mortality is more than doubled, and if labour occurs during failure the mortality is about 50 per cent.

Special advice should be given in regard to hours of rest. The physiological strain of pregnancy on the heart can best be compensated for by increased rest and limitation of exercise. Fourteen hours a day in bed are necessary for all cases, and this should be increased as the pregnancy progresses or if the patient is unusually dyspnoeic. At the earliest sign of cardiac failure absolute rest in bed is necessary.

The physiological gain in weight during pregnancy is an added burden to the heart and should be controlled by suitable restrictions in diet. If the patient is obese efforts should be made to prevent any gain in weight, and in the co-operative patient an actual reduction in weight may be obtained.

The importance of avoiding intercurrent respiratory infection should be stressed, and when slight colds occur the patient should remain in bed.

The occurrence of signs or symptoms of the late toxæmias of pregnancy warrant hospital treatment. J. Corwin *et al.*<sup>6</sup> have reported an increased incidence of toxæmia in the pregnant patient suffering from heart disease, but this has not been our experience. However, the occurrence of even mild degrees of hypertension and albuminuria should be viewed with alarm.

*Management during Labour.*—The occurrence of labour in the patient suffering from heart disease may be looked upon as a final test of the diseased myocardium, yet it need not be unduly feared. If a patient goes through pregnancy without developing cardiac insufficiency then she is very unlikely to develop it as result of normal labour. It is often amazing how well a patient stands a prolonged first stage of labour

without cardiac embarrassment. Cæsarean section has been advocated for a number of years as a method of delivery to relieve the heart from the strain of labour. While the incidence of Cæsarean section has been markedly reduced in our clinic we do feel that it has definite, if restricted, indications, in cases of heart disease. It is justified in patients who have serious myocardial damage and where long or difficult labour is anticipated with increased risk to the baby. The type of Cæsarean section performed depends to a great extent on the degree of circulatory embarrassment that is present. Classical Cæsarean section can be performed with the patient flat on the table or with the shoulders raised. This position is preferable to the Trendelenberg position required for the low Cæsarean. If, however, there is little circulatory embarrassment and the patient is not dyspnoeic, the low section, because of greater safety and less post-operative distension, should be employed. Sterilization should be done at the time of operation.

During the first stage of labour the chief attention should be directed to the relief of pain and anxiety and the promotion of relaxation and rest. Heroin in twelfth of a grain doses, in our experience, has proved the most satisfactory sedative. Morphine and hyoscine are not used because of their occasional exciting effect. In the more prolonged labour adequate intake of fluids and carbohydrates is important to prevent acidosis.

The exhausting expulsive efforts of the second stage of labour should be eliminated by the use of forceps in the full-term deliveries, and episiotomy alone when the child is premature. The anaesthetic of choice is ether combined with oxygen to prevent cyanosis.

Premature labour is a common occurrence and the incidence of excessive post-partum bleeding and haemorrhage is definitely increased. Sudden collapse after delivery may occur. This should be anticipated by the application of a tight abdominal binder with pad after delivery and the early return of the patient to bed in the Fowler position.

*Management during the Puerperium.*—The cardiac patient requires close observation during the puerperium, as frequently two to three days after delivery a period of exhaustion occurs and the patient appears more ill than at any time during the pregnancy. The average patient requires three weeks in bed and the more severe cases, a correspondingly longer time. There is no

reason, if the patient is not too exhausted, why she should not nurse her baby.

#### THE TERMINATION OF PREGNANCY

A discussion of pregnancy complicated by heart disease would be incomplete without considering the indications for the termination of pregnancy. During the past five years, at the Toronto General Hospital, 11 patients have had their pregnancies terminated because of rheumatic heart disease. The indications for termination are shown in Table IV and require little

TABLE IV.  
INDICATIONS FOR TERMINATION OF PREGNANCY  
11 CASES

<i>Indication</i>	<i>No. of Cases</i>	<i>Primiparae</i>	<i>Multiparae</i>
Impending failure.....	4	0	4
Failure before or during pregnancy.....	6	1	5
Toxic vomiting plus heart disease.....	1	0	1
Total.....	11	1	10

comment. The four patients who had their pregnancies terminated for impending failure were all multiparae who, despite hospital treatment, failed to improve sufficiently to warrant the risk of carrying the pregnancy to the period of viability. The history of previous myocardial failure or the occurrence of failure during pregnancy were the indications for termination in six cases. One patient had her pregnancy terminated because of the added complication of pernicious vomiting.

Just as it is impossible to lay down positive dogmatic rules for the management of the pregnant patient suffering from heart disease so it is impossible to be positive as to all indications for the termination of pregnancy. Termination of pregnancy is indicated in any patient who has had myocardial failure before becoming pregnant. There is no reason to believe that a heart which has already failed will stand the added strain of pregnancy. The occurrence of myocardial failure during pregnancy is also an indication for termination, but only after recovery from the failure has occurred. Operative interference with pregnancy during failure is almost uniformly fatal. However, once recovery from failure has occurred the pregnancy should be terminated, as the progressive embarrassment of the heart caused by the growing pregnancy may cause another

and fatal attack of cardiac insufficiency. A slight delay in termination, however, is indicated if the pregnancy is close to the period of viability.

A number of patients will, early in pregnancy, develop increasing impairment of their exercise tolerance, often to a marked degree. A certain number of these require termination, and it is in this type of case that the judgment of both cardiologist and obstetrician experienced in the problem of heart disease and pregnancy is of particular value. The parity of the patient presenting such a picture is an influencing factor in arriving at a decision for termination. With the primiparous patient anxious to have a baby an effort should be made to carry the pregnancy to the period of viability. The multipara, the mother of young children, is a very important member of the home and community, and more radical recommendations are justified. Similarly, the amount of rest a patient can obtain during pregnancy is an important factor. This depends on the size of her family, household duties, responsibilities and her ability to cooperate.

The method of termination of the pregnancy depends largely on two factors, first, the severity of the heart disease, and, second, the duration of the pregnancy at the time of operation. Table V shows the methods used in the present

TABLE V.  
METHODS OF TERMINATION OF PREGNANCY  
11 CASES

<i>Method</i>	<i>No. of Cases</i>	<i>Duration of Pregnancy</i>	<i>Results</i>
Dilatation and curettage.....	2	under 3 months	satisfactory
Supravaginal hysterectomy.....	7	4 to 6 months	"
Abdominal hysterotomy and sterilization.....	1	3 months	"
Bag induction.....	1	4 months	"
Total.....	11		

series of 11 cases. The operation of choice is one that combines termination and sterilization with the minimum of shock and disturbance to the patient. In our experience supravaginal hysterectomy has met these requirements with considerable success when the pregnancy is between four and six months. As many patients with heart disease eventually develop menorrhagia removal of the uterus is of prophylactic value. Early in pregnancy dilatation and curettage is a relatively easy and non-shocking oper-

ation, and while sterilization is not accomplished, it is nevertheless, the operation of choice. Abdominal hysterotomy and sterilization conserves the uterus, which is of doubtful value in these cases, but, according to M. Stutz,<sup>7</sup> of the Zurich Women's Clinic, is followed by an incidence of fatal pulmonary embolism thirty times as great as that after full-term delivery. In severe cases of heart disease on the verge of failure, where any operative procedure is hazardous, the introduction of a hydrostatic bag to induce labour is a conservative procedure.

The question of future pregnancy for the patient with rheumatic heart disease must be carefully considered. The intelligence and the ability of the patient to cooperate will determine whether sterilization or only contraceptive advice is necessary. Patients who have had failure or who have moderate impairment of exercise tolerance should be advised against further pregnancies. For the group of patients who have no symptoms or only slight impairment of exercise tolerance, the deciding factor is frequently the economic status of the patient. The higher incidence of myocardial failure developing during pregnancy in a group of public-ward patients compared with a private group has already been mentioned. This difference can be partly explained by the increased rest, greater comfort of home life, and freedom from worry that the private patient as a rule enjoys. Many factors have to be considered, not the least of which is the parents' own view on the matter. It is only fair to the patient to point out the added risk she faces in a contemplated pregnancy, which can be conservatively stated at five times the normal.<sup>2</sup> We do not believe that sterilization is an indication for Cæsarean section. It can be performed with less risk to the patient when she is not pregnant. Vaginal sterilization is preferable in most cases.

It has not yet been definitely shown that

pregnancy *per se* shortens the life of a group of patients suffering from heart disease. The added responsibilities and increased work associated with the care of young children in the home may be of equal importance. Our impression however is in agreement with the conclusion of Gilchrist and Murray-Lyon<sup>8</sup> that repeated pregnancies tend to shorten life and increase the risk of death from cardiac failure.

#### CONCLUSIONS

1. Rheumatic heart disease is a serious complication of pregnancy.
2. Prenatal observation by cardiologist and obstetrician is necessary for the proper management of these cases. The aim of prenatal management is to anticipate and prevent cardiac failure.
3. If cardiac failure does not occur during pregnancy it is very unlikely to develop as a result of normal labour.
4. The employment of conservative methods of delivery in rheumatic heart cases is recommended, while the indications for Cæsarean section are limited.
5. For the majority of patients further pregnancies are inadvisable and termination of pregnancy is frequently justified because of rheumatic heart disease.

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**GONORRHEAL VAGINITIS: RESULTS OF TREATMENT WITH DIFFERENT PREPARATIONS AND AMOUNTS OF OESTROGENIC SUBSTANCE.**—In treating gonorrhœal vaginitis, R. M. Lewis and Eleanor L. Adler found that oestrogenic substance in ethylene glycol given hypodermically was relatively effective when used in large doses; 2,400 international units daily. Eight hundred international units daily proved disappointing. The use of vaginal oestrogenic suppositories (originally 600 international units and later 1,000) proved very effective. Clinical improvement, cessation or great diminution of discharge is nearly always noted after from fourteen to eighteen days of treatment. The administration of oestrogenic substance changes the reaction of the vaginal

secretions from neutral or alkaline to acid. This, the authors believe, is the major factor in eliminating the gonococcal infection. The acidity of the vaginal secretions is easily measured and provides a sure guide by which one can determine whether or not dosage is adequate. Of thirty-three consecutive cases of gonorrhœal vaginitis in children treated with oestrogenic suppositories, thirty yielded negative smears in an average of 20.7 days. Two required twelve weeks of treatment. Five cases are listed as recurrences. No ill effects were encountered. The method is safe and harmless, and the most effective method known for the treatment of gonorrhœal vaginitis in children.—*J. Am. M. Ass.*, 1936, 106.

## COMPLICATIONS OF ARTIFICIAL PNEUMOTHORAX

(A REVIEW)

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THIS review is an attempt to reach an opinion as to the frequency and severity of the complications of artificial pneumothorax. It is important that one should have an opinion on this point because of the gradually growing tendency to induce pneumothorax in cases of minimal disease and without a preliminary period of a few months' observation.

*Pleural Adhesions.*—Table I shows how frequently various operators have failed to induce pneumothorax because of adhesions.

TABLE I.

Author	Number of cases	Number in which pneumothorax was impossible
1	200	90
2	79	25
3	275	85
4	105	24
5	600	120
6	71	21
7	443	112 Percentage
8	150	37 impossible
9	207	53 = 27
10	462	185
11	51	12
12	149	47
13	200	34
14	139	54
15	250	29
Totals.....	3,381	928

Case selection rather than the technique of induction is responsible for the considerable variation in experience shown by the above Table.<sup>16,17,18</sup> It has been frequently observed, and may be accepted as fact, that the greater the duration of disease, the more likely are adhesions to be present. A most striking demonstration of this is afforded by Turner and Collins' series of 40 early and minimal cases with 100 per cent effective collapse.<sup>18</sup>

When pneumothorax has been successfully induced there is, as Table II shows, a large percentage of cases in which complete pneumothorax is prevented by adhesions.

TABLE II.

Author	Number attempted	Number with only partial collapse
7	443	232
19	492	183 Percentage
9	207	75 with only
11	51	37 partial collapse
20	275	125 = 44
Totals.....	1,468	652

This is a high figure and an important one to remember, because the results of treatment are considerably less worth while when only a partial pneumothorax is possible. Again contrast this with Turner and Collins' series.

When thoracoscopic severance of adhesions is contemplated, the surgeon's chief fear is the presence of lung parenchyma in these adhesions; this has been found in two-thirds of one series.<sup>21</sup>

It is quite impossible to tell in advance by x-ray or by any other means whether adhesions will prevent effective collapse or not. Pneumothorax may be successful even when the x-ray reveals a visible thickening of the pleura, and may be impossible when no warning of the presence of adhesions can be detected prior to operation. Once a lung has been collapsed and allowed to expand, re-induction is frequently impossible, but not invariably so.

*Pleural Effusion.*—The frequency of this complication in the experience of several operators is shown in the following Table:—

TABLE III.

Author	Percentage frequency of pleural effusion	Total number of pneumothorax cases
22	25%	63
23	16%	50
24	"over 50%"	101
2	25%	1,400
5	"nearly all cases at some time"	480
17	42%	?
7	28.8%	143

At least half of these effusions are very small in amount and transient, so that part of the variation in experience shown by Table III may be due to variation in the frequency with which these cases are observed fluoroscopically.

In spite of the large number of theories which have been suggested to explain these effusions, there is sufficient evidence to show that they are tuberculous exudates in all or almost all cases.<sup>24,25</sup> Their incidence is greatly reduced in minimal disease, in chronic disease, in low pressure pneumothorax, and by taking every precaution not to damage the underlying lung with the needle point. Conversely, they become much more common and more severe in extensive disease, acute disease, high pressure pneumothorax, and are almost invariable following the accidental production of a pleuro-pulmonary fistula. It is probable that their usual causes are trauma to the lung by the needle point, tearing or separation of an adhesion, or the natural evolution of tuberculosis upon the surface of the lung or pleura. Bard's demonstration of pleuro-pulmonary fistulæ in almost all cases with exudate is especially convincing.<sup>26</sup>

Effusions most frequently appear without causing symptoms, but any of the symptoms of an ordinary pleurisy may be present. They have no important effect upon the prognosis provided they remain clear.<sup>27</sup>

*Purulent Effusions.*—In general, the greater the volume of the effusion, the more acute its onset, and the longer it persists, the more likely it is to become purulent. This transformation of clear fluid to pus has been observed in 12 per cent of 75 effusions<sup>24</sup>, and in 23 per cent of 186 effusions.<sup>28</sup>

Some cases of tuberculous empyema, however, originate as such. The total incidence of

TABLE IV.

Author	Number of pneumothoraces	Number of empyemas
23	50	1
29	30	1
30	62	3
31	250	26
5	480	58
27	344	6
9	154	7
32	151	32
33	142	9
34	226	12
28	265	42
7	331	6
Totals....	2,485	203

empyema in pneumothorax cases has been reported by various authors as in Table IV.

Empyema is always a worrying complication, but many of these cases are so benign that the clinical course of the disease is not disturbed, and with proper treatment many patients recover without much difficulty, or carry pus in the chest for many years without apparent harm. This, however, is never true of the cases with mixed infection. Of Hayes' 32 cases, 18 had died at the time of his report, and only 1 was accounted well. Of Swezy and Schonbar's 7 cases 4 had died and only 1 was well. Of Peters' and Woolley's 9 cases, 3 were in good condition at the time of the report and 4 had died. Some authors have had better success, however. In Matson, Matson and Bisaillon's 58 cases the complication was found to have no serious consequences unless open drainage was established. McKinney<sup>35</sup> had only 1 death in 8 cases, the remaining 7 being restored to full working capacity. One must make some estimate, and it appears likely that less than half the empyema cases when properly treated by aspiration and irrigation have serious consequences. Since the incidence of empyema is 8 per cent, empyema leading to death or serious and prolonged additional disability will probably occur in less than 4 per cent of all pneumothorax cases. Most of the serious cases are secondarily infected.

Empyemas nearly always occur in cases with far advanced tuberculosis and a high degree of collapse.

The frequency of secondary infection empyema in pneumothorax therapy is variously reported as in Table V.

TABLE V.

Author	Number of pneumothoraces	Number of mixed infection empyemas	Died
36	331	4	3
31	250	8	7
37	254	7	?
34	226	2	?
Totals....	1,061	21	

The percentage incidence of mixed infection empyema is therefore about 2. This is included in the 8 per cent total incidence of empyema, and accounts for most of the 4 per cent of serious empyemas.

Most of these mixed infections are thought to be autogenous in origin and to result from lung rupture. They are frequently associated with bronchopleural fistula.

*Hæmorrhage from the Chest Wall.*<sup>22, 38, 39, 11</sup> These are rare complications. The reviewer found only 8 reported cases. One, associated with spontaneous pneumothorax, resulted in death. No doubt minor degrees of haemorrhage into the pleural cavity are not uncommon but produce no consequences of clinical importance.

*Contralateral Effusion.*—A review of the literature to 1929 resulted in the finding of 32 reported cases.<sup>40</sup> The complication is really to be considered as a coincident happening probably unrelated to pneumothorax therapy, and has usually been of little importance unless associated with the extension of contralateral disease.

*Spontaneous Pneumothorax.*—The incidence of this complication has been reported very variably, depending on the observer.

TABLE VI.

Author	Number of pneumothorax cases	Number of "spontaneous" pneumothoraces
41	1,145	10
42	196	4
43	120	7
11	38	3
31	150	4
9	207	8
5	480	16
23	50	1
44	150	4
17	143	10
22	63	4
Totals.....	2,742	71

The percentage incidence from Table VI is 2.6. There is little doubt that "spontaneous" pneumothorax is much more frequent than this, but, resulting in no serious consequence, is overlooked.

Most of these cases are not really "spontaneous". A better word is "accidental". They may be due to a needle injury, in which case symptoms may be absent or trivial and usually delayed a few hours or minutes. Such injuries will be more frequent at initial insufflations. Or an adhesion may be torn from the lung, when symptoms may be more severe, perhaps resulting in a secondary infection empyema or in valvular pneumothorax.

Mortality from accidental or spontaneous pneumothorax results from empyema or from valvular pneumothorax whose constantly increasing pressures produce circulatory embarrassment and surgical emphysema. Valvular pneumothorax, however, may be classed as a very rare

complication—probably rarer than fatal gas embolism—and the majority of spontaneous or accidental pneumothoraces are harmless.

*Contralateral and Transmediastinal Pneumothorax.*—With an artificial pneumothorax on one side a spontaneous pneumothorax on the other has serious possibilities. Fortunately it is very rare. In 1919 Duboff could find no case in the literature. Since then Burrell<sup>45</sup> has reported 2 cases, both fatal. Walsh's case was also fatal.<sup>46</sup> The reviewer found 5 cases reported in which air escaped from the pneumothorax side into the contralateral pleural cavity. Four of the 5 recovered.<sup>47, 48, 9, 50, 51</sup>

Similar in nature and consequences are those cases of bilateral artificial pneumothorax in which spontaneous or accidental pneumothorax occurs. Since we believe these accidents are fairly common in unilateral pneumothorax they may be expected to be twice as common in bilateral pneumothorax, and no doubt will more readily produce symptoms. The majority of the reported cases have recovered.<sup>52, 53, 54, 55</sup>

*Mediastinal Hernia.*<sup>28, 56, 57, 58, 59, 60, 61</sup>—This term was introduced by Dumarest and Brette. It means a bulging of the mediastinal parietal pleura across the midline through the anterior weak spot of Nitsch, as a rule, thus enlarging the pneumothorax cavity at the expense of the opposite lung. The condition is usually detected by x-ray examination, especially by fluoroscopy, when the herniated portion is seen to be larger with expiration and smaller with inspiration. These hernias occur in young people with healthy, unfibrosed, mediastinal septa. If the pneumothorax pressures are kept low they become smaller, disappear, and do not recur. They are generally harmless. One case is reported, however, of death due to pressure upon the heart and cardiac failure.<sup>60</sup> This complication is unusual, but not really rare, and almost never gives serious trouble. The hernia has however been known to rupture into the opposite pleural cavity, producing a transmediastinal pneumothorax.

Pollock and Marvin have recently reported some cases which they believed to show a collection of air in the mediastinum with bulging of each mediastinal pleural septum to its respective side, and without subcutaneous emphysema in the neck. They believe that cases previously called mediastinal hernia were really mediastinal emphysema or pneumatocele. They may be right. Their paper is quite convincing and should be read by those interested.

*Subcutaneous Emphysema.*<sup>22, 62, 63, 64, 65</sup> — This is a very frequent accompaniment of the initial insufflation, and is almost always no more than a minor annoyance. It is quite unusual after an ordinary refill. It probably results as a rule from tearing the parietal pleura when a blunt trocar is pushed through it. Air may reach the mediastinum by way of the sub-pleural tissues and cause severe dysphagia or crepitations felt beneath the skin of the base of the neck in front. Subcutaneous emphysema may follow a spontaneous pneumothorax of the valvular type, when it becomes extreme, the whole body being swollen with subcutaneous air. Such cases are usually fatal, but are very rare.

*Fibrin bodies in the Pneumothorax Cavity.*<sup>66, 67, 68, 69, 70, 71</sup> — Single or multiple balls of fibrin, usually about 4 cm. in diameter, are occasionally discovered by x-ray loose in the pleural cavity or attached in that part of the pleural cavity most dependent in the usual position of the patient. The patient may be conscious of the internal knocking about of these balls, but usually they are unnoticed and of no clinical importance. A history of effusion is almost always present, and it is thought that the balls consist of fibrin, left unabsorbed when a serofibrinous effusion disappears. Some have been thought to be fibrin from an incompletely absorbed hemothorax. Some appear to persist indefinitely. Some at least are absorbed completely.

*Intercostal Pleural Hernia.* — A unique case is reported by Matson, Matson and Bisailon.<sup>5</sup>

*Pneumoperitoneum.*<sup>72, 73, 74, 75, 76</sup> — This is a rather rare complication. It may be produced by the operator who pushes his needle through an unusually high diaphragm; or air may leak from the pleural cavity through an opening in the diaphragm—probably as a result of congenital defect. Only about 12 cases have been reported to date, and none have produced more than a transitory discomfort, though occasionally pneumoperitoneum has frightened the operator into discontinuance of pneumothorax therapy. Theoretically and usually paradoxical manometer readings will be obtained with the needle point in the abdominal cavity, but this has not been an invariable experience. Neither Zink nor Gerber found paradoxical readings. It is worth remembering too that paradoxical readings may rarely be obtained from the pleural cavity. It is possible that some of the cases reported as pneumoperitoneum may have been subdiaphragmatic rather than intraperitoneal collections of air.

*Pleural Reflex or Gas Embolus or Both.* — Alarming symptoms at the time of operation may be classed as syncopal, convulsive or paralytic. The possible causes for alarming symptoms at this time are:—a simple faint; extreme nervousness; reaction to local anaesthetic; pure coincidence, e.g., insulin reaction, cerebral thrombosis; pleural reflex; gas embolus to the brain or coronary arteries of heart. Convulsive or paralytic symptoms are usually blamed on either gas embolus or pleural reflex, depending on the faith of the operator. Syncopal reactions and very sudden deaths have often been ascribed to pleural reflex. But some believe that all severe reactions not due to coincidence are due to gas embolism, and that pleural reflex either does not exist or is of no real importance. This school of thought is the one most acceptable to the writer.

The evidence for and against the various theories is too extensive to produce here at length. Certain facts however should be known. (1) In nearly all cases, possibly in all, there are adhesions which keep the lung close to the chest wall. (2) In many cases symptoms will be accompanied by bloody sputum as evidence of lung injury. (3) These accidents are more common at initial insufflations than at refills. It seems probable that these accidents are associated always with injury to the lung itself or to adhesions crossing the pleural cavity. No precaution therefore, is too great to adopt in order to avoid lung injury so far as is possible. When recovery occurs from these accidents it is always complete; no residual paralysis persists. Death may be delayed for as long as 7 days, but once consciousness is fully regained recovery is certain.

The frequency with which these accidents have occurred is shown by the following Tables.

TABLE VII.

Author	Number of pneumothoraces	Number with alarming symptoms	Deaths
77	1,400	1	0
78	300	2	1
79	202	1	0
45	344	2	1
5	480	19	2
9	207	3	1
20	275	0	0
80	100	1	0
81	418	10	3
Totals.....	3,726	39, or 1.1%	8, or 0.2%

TABLE VIII.

Author	Number of punctures	Number with alarming symptoms	Deaths
78	8,258	2	1
30	900	0	0
82	7,000	0	0
45	2,332	2	1
83	1,986	9	1
84	12,700	16	7
5	12,000	19	2
85	2,000	11	1
86	10,000	0	0
81	12,000	10	3
Totals . . .	69,446	69, or 0.1%	16, or 0.02%

*Puncture of the Heart.*<sup>42, 80, 83</sup>—This is a very rare event, from which the patients have all rapidly and completely recovered.

*Neuralgia and Neuritis.*<sup>87, 88</sup>—Patients not uncommonly have complained of pain in the neck, in the face or shoulder, down the arm, or in the side of the chest following refills. Some authors have reported such cases as "neuralgia" or "neuritis". These cases are at least generally explicable as due to referred pleural pain, possibly resulting from stretching of an adhesion. It is an unimportant though occasionally an annoying complication.

*Hæmoptysis.*<sup>89, 90</sup>—Spitting of a little blood may follow within a few minutes or hours of insufflations in which it is possible that the needle has entered the lung. Apart from this accident however there are rare cases in which pneumothorax appears to precipitate or aggravate true hæmoptysis. Matson, Matson and Bisaillon<sup>89</sup> have noted that such hæmorrhage may come from the contralateral lung, and urge less compression if this be so, and more compression if the hæmorrhage comes from the collapsed lung.

"*Refil Reactions*".<sup>42, 91, 92, 93, 89</sup>—These are unusual, but are characterized by the occurrence a few hours (4 to 24) after each of several successive refills of fever and possibly of chills, sweats and chest pain. The symptoms persist for 24 to 48 hours. They appear to occur usually in persons who have a pleural effusion, or who have suffered an acute pleurisy at some time. As a rule, but not invariably, they occur rather late in the course of treatment. No satisfactory explanation of their occurrence has been provided, but reactions can often be prevented in cases in which they occur by insisting that the patient stay in bed for 24 hours after each refill, which should be administered to the patient in his bed. They are not of much importance, and should

not often lead to discontinuance of pneumothorax treatment.

*Displacement of the Diaphragm.*—Aycock<sup>94</sup> suggests this as the cause of digestive disturbances following pneumothorax therapy. The reviewer adds the suggestion that this may bear some causal relationship to the rare cases of acute dilatation of the stomach occurring in pneumothorax cases.

*Atelectasis.*—By atelectasis one means absorption of air from the lung or a part of it following obstruction by exudate, by kinking, or by pressure, of the bronchi supplying the area of lung affected. Atelectasis is easily produced in a lung by anything which interferes with respiratory movement, from myasthenia gravis to chest injury. It must and does occur in artificial pneumothorax, and will occur in some degree in all cases if adhesions be not present to help keep the lung expanded and moving. It is the end-result of all cases of complete pneumothorax and many cases of partial pneumothorax. Atelectasis is what produces fibrosis in the collapsed lung. It does so because the bronchus to the atelectatic lung, being obstructed, does not rid itself of secretions, and so non-tuberculous infection becomes active, producing fibrosis and even bronchiectasis in the collapsed part of the lung. Atelectasis therefore is the chief factor responsible for failure of the lung to re-expand, or for its smaller volume when expanded. Adhesions which prevent atelectasis are therefore not absolutely without their redeeming feature. Partial pneumothorax, in which considerable lung movement is permitted to continue, is often found not to result in atelectasis, and this is a good argument in favour of this form of collapse therapy. It is not possible to say how frequently atelectasis leads to serious troubles. If there be a price to pay for atelectasis it is nearly always worth paying.

*Metastatic Tuberculosis.*—Pneumothorax therapy does not completely prevent the spread of tuberculosis to other organs of the body—a spread which must as a rule be haematogenous. Peters<sup>20</sup> reports that extrapulmonary foci developed or became manifest during the course of pneumothorax treatment in 6.4 per cent of 275 cases. Neuer<sup>95</sup> has claimed that pneumothorax therapy actually favours the spread of tuberculosis to other organs. An apparently haematogenous spread of tuberculosis to the opposite lung has been observed by several. A predisposition to haematogenous spread due to pneumothorax

treatment seems distinctly contrary to one's experience, but a doubt has been raised here which, so far as the reviewer can discover, has not been satisfactorily resolved. Here is a study which someone should undertake.

*The Contralateral Spread of Pulmonary Tuberculosis.*—Cooper and Stallings<sup>81</sup> have a report which is particularly valuable because they distinguish between disease originally unilateral and disease originally bilateral. Their Table follows.

*Acute Dilatation of the Stomach.*—This is to be classed as one of the rarest complications of artificial pneumothorax. Shore's<sup>98</sup> case in 1926 is the only one in the literature that one could discover, but the reviewer had one in his practice. Both were fatal and undiagnosed in life. The chief symptom in both was extreme dyspnoea. There was no vomiting or abdominal pain in my case, though both were present in Shore's. This complication should be suspected in any case of

TABLE IX.

	No. of cases on pneumothorax	Unilateral Tuberculosis				Bilateral Tuberculosis				Other Lung		
		No. of cases	Improved	Un-improved	Spread to other lung	No. of cases	Improved	Un-improved	Worse	Better	Unchanged	
Satisfactory Collapse	205 49%	104 57%	54 52%	50 48%	15 14%	101 43%	56 55%	45 45%	21 21%	28 28%	52 51%	
Unsatisfactory Collapse	213 51%	78 43%	22 28%	56 72%	7 9%	135 57%	38 28%	97 72%	41 30%	19 14%	75 56%	
Total....	418	182 43%	76 42%	106 58%	22 12%	236 56%	94 40%	142 60%	62 26%	47 20%	127 54%	

Thus they find a spread to a previously normal lung in 12 per cent of 182 pneumothorax cases and extension of disease in the better lung in 26 per cent of 236 cases. Rist<sup>97</sup> finds that contralateral extension accounts for 75 per cent of the deaths that occur under pneumothorax treatment.

We know that pulmonary tuberculosis tends rapidly to become bilateral if pneumothorax is not induced, so rapidly that the majority of cases are bilateral and far advanced when first they present themselves to the physician. It seems unfair therefore to blame pneumothorax for causing contralateral extension of disease. Unfortunately, however, the reviewer has been unable to find a study of the bilateralization of disease in which pneumothorax cases are compared with control cases. Another doubt has been raised here which needs to be resolved, and here is another chance for someone to make a valuable study. But one must feel that since it can be thoroughly proven that pneumothorax has a favourable influence on the whole, it cannot on the whole favour the spread of tuberculosis.

*Tuberculosis of the Larynx*<sup>98</sup>.—Pneumothorax almost invariably has a favourable effect on this complication when present, and the abolition of bacilliferous sputum by pneumothorax will tend to prevent its development.

severe dyspnoea. Once suspected, it is probable that abdominal enlargement will be observed.

*Diabetes Mellitus.*—This offers no obstacle to pneumothorax treatment, but on the contrary is an indication for the early induction of pneumothorax, in order to shorten the period of toxæmia which will aggravate the diabetes.

*Pneumonia and Influenza.*—Burnand<sup>99</sup> had 20 pneumothorax patients with influenza during the epidemic of 1918-19. Six of these died of "flu"; the remainder recovered, and their tuberculosis was none the worse for their experience. Rickman<sup>100</sup> had 2 pneumothorax patients with pneumonia, and in both the tuberculosis was adversely affected.

Pneumonia of the contralateral lung is a serious situation, and, since pneumonia is a fairly common disease, its possible occurrence is a valid argument against carrying on pneumothorax an unnecessarily long time.<sup>42</sup>

*Pregnancy and Delivery.*<sup>101,102</sup>—The patient with pneumothorax suffers no added risk according to the fairly large series of cases so far reported.

*Digestive Disturbances and Loss of Weight.*<sup>9</sup>  
<sup>103,94</sup>—These occasionally occur following pneumothorax therapy but are rarely of much clinical importance. Three theories as to their cause have been suggested, namely, displacement

of the mediastinum, or of the diaphragm, or a metabolic disturbance due to deficient oxygenation of the blood. The mechanical causes appear to be the most important.

#### SUMMARY

Complications of pneumothorax which lead to serious consequences do so as a rule by causing empyema.

The incidence of empyema having serious consequences is about 4 per cent of all pneumothoraces. The incidence of other serious complications is probably less than one half of 1 per cent, if all are added together, so that serious and probably fatal complications of artificial pneumothorax may be expected in not over 5 per cent of all pneumothorax cases. This is not a minimal figure and may be considerably too high, for Matson, Matson and Bisaillon<sup>19</sup> say of their large group, "of this series less than 2 per cent died of complications related to the pneumothorax treatment".

Since the great majority of empyema cases occur in persons with far-advanced tuberculosis, the risk to an early case is probably less than 2 per cent from all complications of pneumothorax treatment.

In deciding whether or not to induce pneumothorax to such cases this risk is to be balanced against what the individual patient stands to gain by this treatment. The above figures disregard the faint possibility that pneumothorax may actually favour the spread of contralateral or metastatic tuberculosis.

It is to be noted that in 27 per cent of cases pneumothorax treatment has been found impossible because of adhesions, and in another 44 per cent the pneumothorax produced was made only partially effective because of adhesions. Adhesions are very much less frequent, less numerous, and less troublesome in disease of short duration and little extent.

M. Loret records four cases of typhoid fever which occurred during the Abyssinian campaign in Italian soldiers who had been inoculated against the disease. The attack in each case was so modified by inoculation as to be mistaken in two cases for influenza and in one for rheumatic fever. Three developed intestinal perforation, of whom two died, and the fourth patient died

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NOTE: The complete bibliography may be obtained on application to the Academy of Medicine, Toronto.

from intestinal haemorrhage. Loret points out that every physician and surgeon, especially in war time, should consider the possibility of a typhoid perforation in the presence of an acute abdominal emergency, although the patient has been only slightly feverish and the symptoms are indefinite.—*Rif. Med.*, June 20, 1936, p. 858. Abs. in *Brit. M. J.*

## EMBOLISM AND SUDDEN THROMBOSIS OF THE ARTERIES OF THE EXTREMITIES

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SUDDEN occlusion of one of the large arteries of an extremity does not occur often, but when it does it is serious and often results in some permanent disability to the patient, and even may cause loss of the limb. The seriousness of the results is not attributable to the occlusion of the artery *per se*, but rather to the resultant ischaemia of the peripheral tissues which is consequent on the cutting-off of the blood supply. Thus, the results vary with the site of occlusion, the available collateral circulation, the duration of ischaemia and, to some extent, with the rapidity of occlusion.

As ischaemic tissues die within a few hours after the blood supply has been shut off completely, an early diagnosis of arterial occlusion in a limb must be made if one is to attempt to reestablish adequate blood flow to the part and prevent necrosis. In order to make this diagnosis a correct knowledge of the signs and symptoms of sudden arterial occlusion is necessary.

### ETIOLOGY

The specific etiological factor in the sudden occlusion of an artery of an extremity is not always self-evident, and a careful study of the available facts must be made in attempting to arrive at a correct diagnosis. In the presence of the factors to be described subsequently, the diagnosis is often fairly simple. Unfortunately, however, one is not always able to determine any obvious cause, and the conclusion arrived at is a result of logical deduction based on all available information. Fortunately, the treatment of sudden arterial occlusion does not demand an accurate knowledge of the cause.

Emboli which involve the acral arteries originate somewhere in the proximal portion of the arterial tree, in the left side of the heart, or in the pulmonary veins, except the occasional paradoxical embolus, which occurs when a patent foramen ovale is present. The pulmonary veins

are rarely the source of emboli.<sup>1</sup> Mural thrombi in the heart, which are the result of endocardial lesions, are acknowledged generally to be the most frequent source of arterial emboli. Bull, of Riks Hospital, Oslo,<sup>1</sup> in 6,140 necropsies found that 243 (about 4 per cent) of the patients had mural thrombi, and in 9 of these thrombi likewise were found in the aorta. Willius<sup>2</sup> said that about 25 per cent of the patients who die of heart disease have had emboli at one time or another. Willius recognized that factors other than endocarditis played important rôles in the formation of cardiac thrombi (potential emboli); he mentioned such factors as enlargement of the cavities of the heart and disturbances of rhythm. A feeling is developing among some cardiologists that sudden restoration of a normal cardiac cycle in an arrhythmic heart does not predispose towards embolism. Bull found, at necropsy, that the majority of patients who had cardiac thrombi also had pathological changes in the cardiac valves or in the myocardium, and that in all cases in which there were cardiac thrombi there was a greater or lesser dilatation of the various cavities of the heart. The proximal arteries are less commonly the source of emboli. The aorta is the chief source in the proximal arteries, particularly in cases in which emboli are associated with, or are the result of, some specific cause, such as damage to the intima, which may be caused by an aneurysm, arteriosclerosis, or trauma.

Thrombosis of an acral artery actually occurs secondarily to some primary process in the vessel or blood, such as embolism, degenerative processes in the wall of the vessel, inflammation, trauma, or increased coagulability of the blood.

In thrombo-angiitis obliterans sudden occlusion of the peripheral arteries occurs in about 11 per cent of the cases; the percentage is about the same in thrombo-arteriosclerosis obliterans. Why the thrombosis occurs suddenly in this small percentage of cases is not known. In periarteritis nodosa the thrombosis occurs over a period of

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days, but, generally speaking, the condition is more or less acute, and for this reason it has been included in this group. In severe infections, such as peritonitis, pneumonia, septicæmia, and so forth, a bacterial arteritis may play a major rôle in causing thrombosis, but another factor that must be considered seriously is increased coagulability of the blood, which is the result of the infective process. Blood dyscrasias such as thrombophilia, as described by Nygaard and Brown,<sup>3</sup> which tend toward the formation of thrombi, also must be thought of in the differential diagnosis.

Thrombosis may occur in an extremity following operation, and in trying to discover the specific cause there are many factors that have to be considered. Extension of thrombosis from small arteries close to the field of operation to the larger arteries may be the explanation in some cases. However, this does not explain the sudden thrombosis of a vessel distant from the site of operation. In these cases it is possible that increased coagulability of the blood plasma, particularly if the patient is debilitated, may be one of the factors, and stagnation of the blood, which is attributable to inactivity of a limb subsequent to an operation, is probably one of the accessory causal factors when associated with unusual conditions present at the time of operation, such as severe infection, arteriosclerosis, and so forth.

In the presence of gunshot wounds, stab wounds, cervical ribs, or other similar conditions which may injure an artery the thrombosis of that vessel may be attributed to the factors mentioned. Greenspan has described carcinomatous involvement of pulmonary arteries, and it seems logical that carcinoma could invade the wall of an artery elsewhere in the body and cause sudden thrombosis of that vessel.

#### PATHOLOGY

The pathological changes which occur in a limb that is the site of a sudden arterial occlusion may be divided into two groups: (1) those which occur in the limb, and (2) those which occur in the vessel at the site of obstruction. The changes which occur in the limb are the result of the ischaemia rather than the result of the thrombus or embolus. They will, in consequence, vary from simple trophic changes in the skin, nails, and hair, in cases of mild thrombosis, to massive dry or moist gangrene in cases of more severe thrombosis. The changes in the vessel in the region of

the occlusion vary according to the nature of the occluding factor. Thus, in the presence of inflammation, such as thrombo-angiitis obliterans, periarteritis nodosa, and bacterial arteritis, signs of inflammation are present microscopically and even macroscopically. In cases in which arterial occlusion is not associated with inflammation, as in the presence of an aseptic embolus or thrombosis of haemorrhagic origin, the reaction is mild.

Consequent to the formation of a thrombus, and providing the wall of the vessel has not undergone excessive degeneration, according to Muir, fibroblasts and small blood vessels which invade the clot from the intima and vasa vasorum cause organization of the clot, and often re-canalization of the lumen to a greater or lesser degree.

In experimental work on embolism, Gosset, Bertrand and Patel<sup>4</sup> demonstrated that septic emboli caused a marked inflammatory reaction around the clot and in the wall of the vessel at the end of twenty-four hours. Aseptic emboli, in a series of studies made up to eight days after the onset, showed what the authors believed to be aseptic necrosis of the wall of the vessel. This was caused partially by interference with the blood supply of the vascular wall as a result of pressure by the embolus itself. Organization and fibrosis of the clot were well developed at the end of eight days.

#### SYMPTOMS

In 1911, Buerger described sudden arterial occlusion, and described the typical embolic phenomena as being associated with sudden pain, blanching and coldness of the limb. Since then, few other descriptions have been given that have not described the symptoms of sudden arterial occlusion, with particular reference to embolism, as being similar to those described by Buerger. However, a broader view must be taken when entering into a discussion of the symptoms of acute arterial obstruction, as the symptoms frequently are not acute and the condition is not always accompanied by pain.

When an acral artery for any reason becomes completely occluded in an acute manner there is a diminution in blood supply to the distal part of the limb, which is the result of the blockage of the main vessel and the associated arteriospasm in the collateral vessels. Consequent on this sudden anaemia there are phenomena which are attributable to the diminished blood flow to the peripheral bones, muscles, nerves, and other

structures of the limb. These phenomena are readily recognized as associated with ischæmia, even though their specific etiological factor is not always apparent. Similarly, it is impossible to explain the reason why some manifestations are apparent in one case and not in another, or why there is a total absence of signs and symptoms, as in an unusual case of acute occlusion described by Buerger.

In a previous study by the author and E. V. Allen<sup>5</sup> it was shown that the onset of symptoms occurred suddenly in 48 per cent of cases. The remaining 52 per cent had an onset lasting from one to several hours before the maximal severity of the symptoms was present. In 54 per cent of cases, pain, which rarely was of great severity, was the initial complaint, and in 44 per cent of cases the pain came on suddenly. Other symptoms of less frequent occurrence were tingling, tenderness, cramps, itching, pallor, and burning, in the order of their frequency.

There was no definite order of onset or apparent causal relationship in the presence of these individual symptoms, and they occurred singly or in varying combinations with each other, one or the other predominating in different cases. Thus, an attempt to describe the clinical symptoms would be difficult, other than to say that the presence of any of these symptoms should necessitate a further study of the case, particularly in relation to the objective findings of the cardiovascular system.

The examination of the patient usually shows that there are few if any signs of shock unless the unusual severe type of pain is present. The facial colour is fairly good, the pulse is a little faster than it normally is, but, unless cardiac decompensation is present, the rate is not alarming. The oral temperature is within normal limits, and the patient is usually wide awake, alert, and somewhat apprehensive. The appearance of the limb readily demonstrates that some pathological change has taken place. The normal colour is absent and the limb is blanched, blotched, or sometimes slightly cyanotic below the region supplied by the available collateral circulation around the obstruction. The veins are collapsed, the limb is frequently immobile, and its general appearance is very aptly described as lifeless.

Palpation reveals the skin to be cool and moist, and no pulsations are felt in the arteries peripheral to the site of obstruction. Tests for sensation, muscular power, and neurogenic reflexes ordi-

narily show diminished or absent responses. It is a definite clinical impression that the degree of anaesthesia, paresis and diminution of reflexes depends on the degree of ischæmia, and that the amount of response in an affected limb is in proportion to the blood supply, providing the response is not produced by structures situated in a region which has a good blood supply and which is proximal to the anaemic portion. Assuming this impression to be true, then the amount of voluntary muscular movement might be used as a rough index of the amount of collateral circulation functioning. That this is logical is borne out by an observation made by Allen<sup>10</sup> that the complete absence of digital movement in the involved extremity probably means that little or no collateral circulation is present, and that the chances for recovery of the limb are slight if paresis persists a few hours.

If the blockage of the artery is complete, and if there is insufficient collateral circulation to maintain life in the tissues, then within the first few hours the sensations of pain, numbness, and tingling usually diminish or disappear altogether, and the patient complains only that the limb is "dead" and that he is unable to move it. If pain, tingling, and movement are present after the first few hours, they are either in the proximal portion of the limb, where some circulation is present, or there is sufficient collateral circulation to the more distal parts to allow for the continued viability of some nerve fibres at least. After a lapse of several hours a retrograde flow of blood occurs through the venous channels, which progresses slowly peripherally, and which frequently changes the colour from pale whitish to a blotchy bluish purple. This retrograde seepage is of no significance and does not indicate the restoration of circulation.

Death of the tissues is the ultimate outcome if the cutting-off of the circulation is not compensated for quickly. This necrosis manifests itself as gangrene. If, however, sufficient circulation is reestablished the limb may recover to the extent where it is a functioning member once more, although it seldom recovers sufficiently so that there are no residual symptoms, such as varying degrees of claudication.

#### DIAGNOSIS

As the deleterious effects of arterial occlusion are the result of ischæmia of the tissues, the final results of obstructing the blood supply to the

limit will vary in accordance with the degree and the length of time the blood supply is diminished. Thus the diagnosis obviously must be made early if benefit is to be derived from treatment. In order to make the diagnosis early it is not necessary for the physician to have an accurate and widespread knowledge of the symptoms and pathology of sudden arterial occlusion. Rather, all that is necessary is the knowledge that the symptoms are sufficiently varied, so that if some unusual occurrence directs his attention to the limb he will carry out a thorough examination, particularly of the acral arteries, and will rely on the examination rather than on the history for the diagnosis of occlusion.

An embolus most frequently is arrested at the bifurcation of an artery where there is a sudden diminution in the size of the vessel. The bifurcation of the femoral and popliteal arteries is the most common situation in the legs, and the bifurcation of the brachial artery is the most common situation in the arm. Absence of pulsation below a given point in an artery is indicative of arterial occlusion, if a normal arterial tree always is assumed to begin with. If this absence of pulsation is associated with abnormal pallor and decreased surface temperature, then the diagnosis of recent arterial occlusion is justified. Other findings are confirmatory but not individually diagnostic.

The differential diagnosis lies chiefly with anomalies of the vascular tree, in which the arteries of the extremities do not follow their normal course, and with arteriospasm. In the former condition there are no other significant findings which indicate an associated pathological closure. In the latter condition, however, the differentiation is not so simple. Küttner and Baruch<sup>6</sup> described a case in which the ankle was injured by a bullet and the posterior tibial artery was thought to be thrombosed, as signs of obstruction were present. While the wound was being repaired, the vein was found to be injured; the artery was uninjured but in a state of spasm which completely occluded its lumen. Montgomery and Ireland reported two cases of traumatic arteriospasm of the brachial artery, and gave an excellent review of the reported cases of this condition. Ordinarily, a careful study of the possible etiological factors and the subjective and objective findings will lead to the correct diagnosis.

### PROGNOSIS

The prognosis in sudden peripheral arterial occlusion is not always good, as I have found that gangrene developed in about half of the cases studied in which there was sudden occlusion. Of those patients who did recover there were very few who did not have at least some residual symptoms, such as claudication, trophic changes, and so forth.

### TREATMENT

The treatment of an extremity subsequent to the sudden occlusion of an acral artery has changed considerably in recent years as a result of a more thorough knowledge of the course of events. This knowledge, which has been gained by careful clinical and experimental investigations, is the basis of present-day treatment.

Gosset, Bertrand and Patel<sup>4</sup> observed arteriospasm in the region of an artificially produced embolus. They also noted that the surface temperature (as indicative of circulation of blood) was restored to normal after several hours in many cases. Mulvihill and Harvey,<sup>7</sup> in experimental ligations of the femoral arteries of dogs, found that the usual decrease in the surface temperature of the limb could be prevented or promptly compensated for by paralysis or section of the sympathetic nerves to the part. Herrmann and Reid<sup>8</sup> have shown that alternating suction and compression on an affected limb has a beneficial effect, and they claim that when there is more or less sudden occlusion of one of the major arteries of an extremity the early use of this form of treatment practically eliminates the possibility of gangrene. Denk<sup>9</sup> reported excellent results in cases of sudden peripheral arterial occlusion in which the patients were treated with papaverine hydrochloride.

One can realize that the measures instituted should all tend to increase the inadequate collateral bed, which is thought to be inadequate as a result of arteriospasm in addition to occlusion. As spasm of the arteries or inadequate dilation seems to be the result of activity of the sympathetic nerves, then procedures that will paralyze these nerves are indicated; these procedures comprise spinal anaesthesia, brachial block, or deep general anaesthesia. Vasodilators, such as papaverine hydrochloride, in doses of  $\frac{1}{2}$  grain (0.032 gm.) administered intravenously, may be tried. Alcohol, 0.5 c.c. per kilogram of body weight, is also beneficial, as shown by Brown and Cook. Other vasodilators, such as mecholin and theobromine have been shown to have definite clinical value. Great care must be taken of the limb itself, and it should be wrapped in cotton and placed under a cradle with the temperature not more than 105° F. It should be remembered that devitalized tissues burn more readily than do normal tissues.

If a prompt response to these attempts at vasodilatation does not occur, then surgical intervention may be considered if the obstruction is the result of an embolus. Mosny, Dumont, and Labey performed the first successful embolectomy in 1911; the next year, Key performed a similar operation. Since then, there have been many arteriotomies performed. In 1929, A. W. Allen<sup>10</sup> reviewed the literature and found that only 25 to 30 per cent of the embolectomies were successful. In 1933, Danzis<sup>11</sup> collected 119 reports of embolectomies from the literature, of which 41 per cent were immediately successful. In these cases, 25.5 per cent of the patients died from embolism which occurred two to eight months after operation. Inasmuch as the surgical technique of embolectomy has been described in an admirable manner by Pemberton,<sup>12</sup> A. W. Allen,<sup>10</sup> Labey, and others, it seems unnecessary to discuss it further in this paper.

The reason for the failure of embolectomy is most frequently the development of a secondary thrombosis. This may occur almost immediately, or not for some time. Ipsen found no evidence of thrombosis two days after the obstruction occurred, whereas Lindberg found a secondary thrombus, 86 cm. long, as early as twelve hours after the onset of the embolism.

Key said that no benefit ordinarily was obtained with operation after forty-eight hours, and that in cases in which operation is performed within forty-eight hours of the onset of the embolism good results may be expected in 45 per cent where the operation is performed one to ten hours after the onset; in 21 per cent in which

it is performed ten to fifteen hours after the onset; and in only 10 per cent in which it is performed fifteen to forty-eight hours after the onset.

#### CONCLUSIONS

1. The symptoms of sudden arterial occlusion are extremely variable. The common conception that severe pain, which ensues suddenly, is the chief manifestation is misleading.
2. Sudden occlusion of an acral artery demands early institution of adequate treatment.
3. Treatment should consist of attempts to overcome arterial spasm and to enlarge the collateral arterial bed. Embolectomy may be tried early in selected cases.

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**KLEIN'S CANCER REACTION.**—H. Horster reports from the University Hospital of Würzburg investigations he has conducted into the reliability of the reaction described by G. Klein of Oppau in September, 1934. After studying Klein's technique Horster arranged to send him samples of blood from Würzburg, and within a year the blood of 215 patients had been examined in Klein's laboratory. There were 75 cases of malignant disease, 125 cases in which tumours could be excluded, and 15 cases in which the clinical diagnosis was doubtful. It was found necessary to exclude from the final analysis several of the cases because they were complicated by adventitious circumstances such as fever, haemorrhage, constipation, cachexia, anacidity, or retention of food. Other circumstances confusing the issue were the ex-

hibition of certain drugs and x-ray examination. After all the cases thus complicated had been eliminated there remained 45 patients suffering from some tumour; among them were 39 positive Klein reactors and 6 which were negative. Among the 91 patients not suffering from tumour were 83 giving a negative Klein reaction and eight a positive reaction. Horster concludes that Klein's tumour reaction does not at present represent a valuable contribution to the diagnosis of malignant disease, largely because of the facility with which extraneous circumstances obscure the issue. To this negative verdict he adds the rider that Klein's reaction promises so much of theoretical and scientific interest that he intends to continue his investigation of it.—*Deut. med. Woch.*, March 10, 1936, p. 460. Abs. in *Brit. M. J.*

## THE PSYCHOLOGICAL DISTINCTION BETWEEN THE VARIOUS TYPES OF SCHIZOPHRENIA

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### INTRODUCTION

THERE is a tendency in studying psychotic cases to restrict attention to the enumeration of symptoms for the purpose of categorical classification and the estimation of prognosis. Even granting that we acknowledge the existence of mental conflicts, complexes, symbolic manifestations, etc., we do not utilize these conditions systematically to explain the type of reaction which the patient is showing. Even granting also that we distinguish certain personality types, we still do not utilize these, except in a very general way, to explain the nature of the disorder. That is to say, our study is largely symptomatic, rather than etiological or interpretive. It is not the purpose of this paper to go into the details of the symptoms in the various groups, but rather to offer some generalizations regarding the psychological processes involved in the development of the various types of schizophrenia. Since we admit that there are different types of this disorder it is surely not too much to suppose that there must be some distinguishing factors in the etiology which lead to the various manifestations.

The study of psychology teaches us that the activity of the normal mind may be analyzed into various factors. In the following pages the growth in the mind of four different processes is discussed, and an effort is made to show that the four types of schizophrenia represent disorders of these four processes.

### PART I.

#### THE SIMPLE TYPE OF SCHIZOPHRENIA INTERPRETED AS A DIMINUTION OF INSTINCTIVE FORCES

(a) *Normal growth of instinctive forces.*—One of the most universal attributes of the animal mind is a tendency to display *interest* and

*energy.* According to the view of most psychologists these are expressions of instinctive forces. In the human infant the development of these forces is gradual. At first he responds mechanically to certain stimuli, such as the opportunity to suckle. Some such experiences bring pleasure and he becomes interested in them and eager to play his part; others he dislikes, and his energy is directed towards avoiding them. The various instincts gradually become more manifest, curiosity, anger, fear, constructiveness, play, etc., etc., and they form the basis of most of the child's activity. As time goes on his innate tendencies become elaborated and directed into more useful lines. He becomes interested in work, he assumes duties and responsibilities, he becomes ambitious for the future and directs his life accordingly.

The course of these developments is naturally dependent on the experiences to which the individual is exposed. His interest is aroused in some lines and thwarted in others. His ambition should develop in keeping with his opportunities; otherwise it is unlikely to be fulfilled. One should note that there is considerable variation in the amount of energy displayed. Individuals differ considerably, some being naturally active while others are more listless. Also, the same person will display much more interest and energy along some lines than others, and even from time to time the amount of energy he displays towards the same subject will vary. Within certain limits, however, such variations are normal.

(b) *Diminution of instinctive forces.*—In the simple type of schizophrenia there appears to be an abnormal diminution of interest and energy. This, after all, is one of the most natural reactions to any unsatisfying existence. If a person is dissatisfied with his circumstances in

life, if he is discouraged by his failure to attain his desires, is not the simplest reaction that of giving up the struggle? The forces which should drive him on diminish or atrophy; he begins to disregard his duties, responsibilities and ambitions, and follows the line of least resistance. One might cite examples of diminution of instinctive forces occurring in so-called normal people as a result of adverse circumstances. Take, for instance, the disappointed lover who loses interest in life for a long time, and possibly never regains the zest which he formerly experienced; or take the wife who, when married to a brutal husband, gradually loses her energy, pugnacity, determination, ambition, even her self-respect, and subsides into a humdrum life of listless submission; or take the ambitious young man who fails repeatedly to obtain the promotion he deserves, and who finally feels discouraged, stops struggling, and accepts a routine occupation which offers a bare livelihood.

In the case of the simple schizophrenic the changes are more severe. He so disregards his responsibilities to himself and others that he is no longer able to maintain any normal position in the community. His earning power decreases, and, with it, his standard of living. His dependents suffer, he loses his friends, and he drifts along. To many people such consequences would be intolerable and would increase the mental conflict. But to this type of individual the consequences mean nothing; his sense of values has changed to such an extent that he has no ambition for higher achievements, and he does not regret his condition nor blame either himself or others for it. His emotions, which should be aroused by his plight, become flattened and his interest and energy diminish. When he reaches the haven of a mental hospital he accepts a placid uneventful existence, and may adopt a simple routine occupation with neither ambition nor resentment. It is to be noted that in this type of case associations are coherent as far as they go, but thinking is reduced to a minimum. The patient's imagination is not active consciously or subconsciously, and there is little tendency to develop delusions or hallucinations. Failure of interest and energy, such as occur in this type, may be regarded as deteriorating factors. The progress of the disorder may become arrested at any point, but recovery of interest and return to normal is uncommon.

(c) *Example of simple type.*

(Case No. 5506 P.M.H.)—This patient is a woman who was admitted on January 5, 1932, at the age of 42. There was no history of nervous or mental disease in her family. She was born in Ontario, and her infancy and childhood were said to have been normal. She attended school until 17, when she failed in one subject in third year high school. She tried nursing, but was discharged over some affair with a disreputable man. Later she worked in a sanatorium. At 22 she married a man who was unattractive and unequal to her in refinement. Her married life was probably not happy. She spent much time reading and day-dreaming about the stories she read, and she neglected her housework. She is said to have been sensitive, stubborn and lazy, but not shy. She had very restricted interests. Some sexual irregularities occurred while she was single.

Her present illness probably started before 1926. In that year she spent six weeks in a mental hospital and is said to have been very erotic. Following this she returned home but never adjusted well. She separated from her husband and she and her three children lived on the allowance she received from him. She made no attempt to improve her circumstances. There was a gradual loss of interest. She became more and more negligent in her housework. She shirked her responsibilities and did not appear to realize that she had any. Even when one of her children was in diabetic coma she neglected his treatment and appeared quite unconcerned.

When admitted to hospital she was in good health. She has been quiet and placid, and has worked steadily in the nurses' home. She is satisfied and entirely lacking in ambition, and shows no initiative to depart from the simple routine of her monotonous life. She shows a shallow mechanical smile when spoken to, and answers questions rationally but without emotion. When not occupied she sits by herself. There is evidence that her thought processes are of a very simple type. She has no delusions or hallucinations.

## PART II.

### HEBEPHRENIC TYPE OF SCHIZOPHRENIA INTERPRETED AS A DISORGANIZATION OF THE MIND

(a) *Normal organization of the mind.*—As an individual's mind develops from infancy to maturity it becomes more and more completely organized. Association is an important factor in this development. Things which occur together or in sequence, or which have similarities, become associated in the mind so that the thought of the one tends to recall the thought of the other. As a result of these associations things take on meanings. The individual learns to appreciate the relationship of various things, their significance, their relative values. It is important to recognize that feelings and emotions determine to a considerable extent the significance which things have for an individual—hence love is blind. Some things become associated with pleasure, some with pain, some with love, some with hate, some with fear, and so on. As various emotions all become associated successively with the same object, such as one's mother, the object develops a complex emotional

significance which is termed a "sentiment". One experience will emphasize one relationship, while another experience may emphasize another relationship. For instance, when the mother feeds her child he associates a certain form of pleasure with his mother; at another time, when she punishes him, he associates fear and pain with her. Now these two associations might conflict were it not that the child should also associate with each case the circumstances in which it occurs. Thus he finds that his mother is good to him when he is good, and strict with him when he is bad. In other words, when adequate and accurate associations are developed, the relationships which result in the mind are consistent; and while opposite emotions may be associated with the same object they do not conflict, because they are reasonable and appropriate to the circumstances. This is to be expected in ordinary life, because one's environment is more or less consistent, being dependent on the laws of nature and the laws of man, and therefore one's experiences are consistent.

Here let it be pointed out that associations are not always the result of experiences with the environment. Some are developed in imagination, as, for instance, when a child imagines that his mother will punish him for some act when actually she might be quite sympathetic. As a rule one's imagination conforms fairly closely to reality, or else one realizes that his fantasy must not be made the basis of reasoning. Otherwise the organization in the mind tends to be less coherent. As years of experience pass, the individual's mind becomes more and more firmly organized. His sentiments, ideals, standards and beliefs become consistent guides to direct his behaviour; and, although always somewhat pliable to the effects of new experiences, the organization normally tends to assimilate such experiences rather than being disrupted by them.

(b) *Disorganization of the mind.*—In the hebephrenic type of schizophrenia this harmonious organization fails. Conflicting rather than consistent associations develop, particularly those of a sentimental nature. Both subconscious and environmental factors may influence this development. Repressed complexes may impel the individual to actions which he cannot harmonize with the standards of those around him. He finds it difficult to adjust his sense of values. Because he wishes something that is taboo he may hate himself at one time for his weakness,

and again he may hate his environment for the restrictions it imposes. Thus conflicting and unsatisfactory attitudes become associated with the same situation. Inconsistent conditions in his environment may add to this lack of organization. For instance, the sentiment of love for a parent may conflict with feelings of hate aroused by unhappy experiences with the same parent. Or the interest in school work may be offset by antagonism to real or imaginary unfairness of the teacher. The pupil may thus fail to develop a normal appreciation of the value of an education, and his life at school becomes dominated by inconsistent sentiments which lead to further unfortunate experiences.

This condition may be aggravated by imaginative processes. The individual may build up in his imagination new and unnatural associations. Introspection makes him even more confused. Because of the conflicting ideas in his mind he has no fixed standards by which to judge his problems. Standards to which he formerly adhered may be shattered by some new experience, leaving him more confused than ever. The systematic structure of his mind becomes disorganized, disintegrated and incoherent. One usually finds that such a patient has had strong emotional tendencies, but has had difficulty in sentimental adjustments. Ideas of affection, ambition, sex, religion, etc., may have been prominent but never satisfactory. The individual may have made strenuous attempts to face life, but with repeated failures. There is often a sensitive, introspective nature, with a feeling of inferiority. Due to the disorganization of the mind, symptoms of incoherence are prominent—incoherence of thought, incoherence of action, incoherence of emotion. The imaginative tendency has not diminished, and hallucinations and delusions are prone to develop. Also, there need be no diminution of energy but a continued effort to combat difficulties with resulting outbursts of feeling or action. The disorganization being progressive, deterioration is usually rapid, and recovery unlikely.

(c) *Example of hebephrenic type.*

(Case No. 5906 P.M.H.)—This girl was admitted on November 16, 1932, at the age of 21. Her father is reported to have been alcoholic and shiftless, and to have deserted the family before the patient was born. At birth the patient weighed three pounds, and she was not robust until in her "teens". Her early development was otherwise normal. She made good progress in school to Grade VII. Then she took three years to get through Grade VIII. She stated she had a poor teacher

and "didn't know what it was all about". She spent two years in Grade IX; she was afraid of herself and felt she could not cooperate with the teacher; she would try to memorize the textbooks. She did better in Grade X, and finally passed most of Grade XI at the age of 20. In the final year she had a good teacher, but she regarded him as her enemy because he was sarcastic and he thought she would not pass; she worked hard to show him that she could.

Up to this time she had lived at home. Her mother, to whom she was greatly attached, died when she was 17, but the patient continued living with her brothers. Although she earned some money in a telephone office she gave that to her brothers. They did not treat her considerately. If she wanted some money she might have a quarter tossed across the table at her. She said she loved one brother, although he criticized her. The other brother, she said, was inhuman. She apparently felt out of place at home and that she was practically told to get out in the end. At the age of 20 she obtained a position away from home. Her work was satisfactory, but she was not altogether happy. Her effort was chiefly to show people that she could succeed. She did not feel at one with her companions, and said she should have given them a piece of her mind and they would have thought more of her. She felt that they "picked" on her. At the end of one year she suddenly broke down and her present illness became manifest.

Before her illness she was considered lively and fond of company, and nearly always happy and placid. She was sensitive. Sometimes she was over enthusiastic and energetic. She had a marked feeling of inferiority. She showed no real self-criticism but a great deal of self-defense. She struggled to succeed, not for the benefit she obtained but to show people she could do it. She felt misunderstood and appeared unable to interpret other people's personalities properly. For instance, she said of one of the girls who tended to be rather abrupt, "I suppose she was trying to show her dirty disposition". She said of another girl, how selfish and how brainy she was, and yet how she liked her. She was surprised that the girls with whom she mixed could say such harsh things. She seemed to have envied other girls who had more excitement, and yet she was outwardly intolerant of undue familiarity or sexual laxness. She admitted having gone to rather wild parties which did not appeal to her, but she went to try to be like other people. After such affairs she would feel disappointed and disgusted with herself. She smoked heavily at times, and occasionally took liquor. She practised masturbation, and had at least one heterosexual experience. At the age of 18 she suffered from goitre and had a nervous breakdown.

Her present illness probably developed insidiously. It would appear that for years she had difficulty in forming her ideals and standards and her opinions of other people and her relations with them. She was harassed by conflicting ideas and obtained no help from others in adjusting them. Her symptoms became manifest suddenly at the age of 21. She became excited and noisy. She had ideas that people were trying to kill her. She said she had a master mind, and expressed other strange ideas about youth and people trying to kill youth. She addressed remarks to God and to people at a distance. Emotionally, she was very changeable, laughing, crying, fearful, euphoric. She showed flight of ideas and some incoherence. She would be concerned about trivialities. For instance she said she was contradicting Shakespeare. He wrote a ballad to Lady Eyebrow, but "You could not write a long ballad to any eyebrow, it is such a small thing, especially when plucked as girls have them these days". She spoke freely of sexual matters.

This patient's condition has become progressively worse. She is extremely hallucinated, violent, destructive, noisy, silly, dirty, profane and vulgar. Her speech is usually quite incoherent, but indicative of bizarre changeable delusions. She has spoken of her hands as being "strangler's hands", "the devil's hands", etc.

She was emotional, tense, and energetic. One always had the feeling that there was something pathetic about her, that she struggled to make good, only to find her mind becoming more and more confused with conflicting ideas until it disintegrated into a jumble of rebellious thoughts.

### PART III.

#### CATATONIC TYPE OF SCHIZOPHRENIA INTERPRETED AS A DETACHMENT FROM REALITY

(a) *Normal attachment to reality*.—Early in his development a child begins to recognize that things about him are real. At first his contact with an object produces only uninterpreted sensations. Gradually sensations begin to have meaning for him. He finds that they are caused by certain things. He learns that these things are concrete; they are real; they exist in a certain position, perhaps at a distance from him; they have meaning; he can expect certain experiences with them. Thus his sensations are no longer uninterpreted, they are elaborated into percepts. He develops a recognition of the concrete world of which he forms a part. He also develops a relationship to this world, a rapport, a condition which keeps him *in contact with reality*. Although one rarely analyzes this relationship, there is in the normal mind no tendency to doubt the reality of the environment. For instance, when awake, one does not normally have any feeling that he is in a dream. There is, however, another form of experience which he must learn to distinguish. He may recall in memory incidents which have occurred in the past. Similarly, he may produce in imagination situations which he never experienced in reality. Nevertheless, he distinguishes between the objective facts of his environment and these imaginative ideas and memories which may come into his mind.

At the same time he learns to utilize his imagination. Ideas may be allowed to run freely in a wish-fulfilling way, as in fantasy; or they may be directed in a constructive way to develop a theory, or solve a problem, or produce a story, or anticipate an interview, or plan a trip, etc. Such imaginings may in many cases excite one's emotions much as the real experiences would. Witness, for example, the erotic excitement caused by voluptuous fantasy, or the tears or laughter produced by reading fiction. Normally, however, one retains his awareness that these experiences are not real and he rarely reacts to them with overt activity.

(b) *Detachment from reality.*—In the catatonic type of schizophrenia the patient ceases to distinguish between what is real and what is imaginary. He loses his rapport with his environment. His focus of consciousness becomes detached from reality and centred chiefly upon his imaginative preoccupations. In this type the personality is not disorganized as in the hebephrenic, but its organization has progressed in more or less opposition to the environment. Many of these patients are of a determined disposition, prone to accept their own views in defiance of the doctrines of others. Some of them are imaginative and dreamy and inclined to indulge in fantasy. Their subconscious impulses are harmonious within themselves and in keeping with their imaginings. That is, an organization has developed in the patient's mind distinct from his overt activity. He recognizes, while normal, the scheme of things in reality, but he also has a scheme of things of his own.

Frequently the onset of the symptoms is sudden, although it is sometimes gradual. The patient ceases to distinguish between the reality around him and the ideas which occur in his imagination directed by his subconscious. His view of his surroundings becomes fogged, and his sense impressions are interpreted in terms of his imaginative preoccupations. He may completely withdraw from reality and go into a stupor, or he may react to his surroundings in a disordered way, guided by his fancies. Many such patients admit that they feel as if in a dream and that their surroundings seem unnatural and sometimes peculiarly altered. The freedom with which imagination acts in this type leads either to vivid fantasies or to actual delusions and hallucinations. These are frequently wish-fulfilling in nature, but distressing, self-accusatory, or paranoid ideas may occur. Owing to the fact that the fabric of this psychosis develops in the imagination and is detached from reality it remains possible for the patient to return to reality and see it again clearly and normally. This accounts for the fact that a proportion of these patients recover. There need be no disorganization and no distortion of reality as in the next type.

(c) *Example of catatonic type.*

(Case No. 6327 P.M.H.).—This patient was a young man of 26 at the time of admission on November 7, 1933. His family history was negative.

His personal history was normal up to the age of 16 when he had an attack of poliomyelitis which left

him with a partial paralysis of the right leg causing a pronounced limp. He stayed at home and attended school at irregular intervals until shortly before admission. He was in Grade XII. His personality had changed considerably as a result of his physical disability. Formerly very fond of sports, he never became reconciled to the limitation of his activities. He became sensitive, independent, and elusive. He was more imaginative, inclined to day-dream, and to brood over his condition. He became irritable and quarrelsome. He admitted masturbation but denied any interest in girls; he felt girls would not be interested in a cripple like him. At the age of 21 he had a so-called nervous breakdown.

Symptoms of his present illness became manifest in September, 1933. He became worried because he anticipated extra work at home besides his school work. He had to give up school and was unable to do anything at home. He felt dazed, and started to hear voices of girls talking about sex matters. After admission to hospital he was usually quiet and cooperative but had occasional impulsive outbursts. He was rather disinterested and chiefly concerned with the voices, which he said he enjoyed. He said they took the place of normal activities in which he could not participate.

The patient had good insight and gave an interesting description of his illness. Its genesis seems to go back to his attack of poliomyelitis ten years ago. His physical disability "killed his interest in sports and other things". He had nothing to keep his "mental vitality up" and he gradually declined. He felt as if people treated him differently. He lost interest in things he was doing and turned to things he imagined. He lived more in his own thoughts; "there was nothing else to do". He day-dreamed, wishing he could get out and do the things other people were doing. When his psychosis became manifest he felt dazed. "It was a sort of sinking feeling, like going down in an elevator with no bottom. It could only be mental because things were still the same". He felt "separated from people, out of touch with them". Friendships and everything had changed. People seemed far away. The world seemed different, but he knew that it was only he who had changed. Sometimes people's remarks seemed to have a meaning out of the ordinary. He was worried because he could not understand things. "I didn't know where I was at." It is interesting to note that when he was more closely in touch with reality, as when he was doing occupational work, he found the voices much less noticeable.

#### PART IV.

##### PARANOID TYPE OF SCHIZOPHRENIA INTERPRETED AS A DISTORTION OF REALITY

(a) *Normal view of reality.*—It is not only necessary that the normal individual should be in contact with reality but also that his view of reality should be clear and accurate. This depends on judgment. Just as the normal lens of the eye focuses innumerable rays of light on the retina, to form a clear picture of the spacial relations of objects, so also normal judgment presents to the mind a clear picture of the relationship of objects and situations in life. Strictly speaking, judgment is based on experience; one recognizes the significance of a situation today because he associates it with similar situations he has experienced in the past. Most

frequently these associations act unconsciously, and one is quite unaware of why he forms a certain opinion. For example, he decides that he likes a certain individual (on the basis of past experiences with him or with others like him) although he is unaware of why he is so attracted. A higher form of judgment is involved when there is conscious reasoning upon which a decision is based. In all cases, however, the accuracy of one's view depends on the appropriateness of the associations which are utilized (consciously or unconsciously).

Certain factors may influence the associations which are utilized, and therefore affect the conclusion drawn. Some prejudice or the mood of the moment may obstruct the natural associations and cause the individual to react to quite inappropriate associations. For example, a teacher who has just had a quarrel with a colleague may see only the faults in her pupils' work and be blind to the good qualities. Or a strong Conservative may criticize some Liberal for discharging an employee, although the Conservative knows nothing about the circumstances; his judgment is based on quite inappropriate associations, *viz.*, the other is a Liberal and therefore wrong. Similarly, subconscious forces may have a profound influence on one's judgment. The man who has repressed a feeling of guilt for some misconduct may consequently be the first to condemn his fellow man for the same offense—his own feeling of guilt is associated with the other man's misconduct and forms the chief basis of his judgment. Thus it happens that, contrary to the logical process, one frequently makes a decision first on the basis of unrecognized associations and then proceeds to justify the decision with plausible explanations. This is the process of rationalization.

Opinions once formed tend to be a basis for future opinions. This is the process involved in learning as well as in many every-day judgments. We think, for instance, that if a man is once a thief he is always a thief, and we judge him accordingly. Erroneous judgments as well as accurate judgments tend to be perpetuated in this way—the reputation of the supposed thief may be false from the beginning. A normal person, however, is usually sufficiently adaptable that his view of important matters is harmonious with the realities of life as he is exposed to them. That is, he has a sufficiently accurate view of his environment to be able to react to it in a satis-

factory manner. His knowledge and beliefs, though not infallible, are compatible with the views of those around him.

(b) *Distortion of reality.*—In the paranoid individual, however, this does not occur. Such an individual is usually energetic and observant of things about him, particularly the actions of others, but he is prone to jump to conclusions and put his own interpretation on things. His judgments are biased. He does not give others the benefit of the doubt.

Due perhaps to repressed wishes or to his own inability to achieve his ambitions, he may become dissatisfied with his circumstances in life. Although unaware of the real cause of this dissatisfaction he adopts a constant attitude of suspicion, self-defense and prejudice, which interferes with his proper view of life. His astigmatic judgment persistently presents situations in a distorted form. This causes him to put the blame on others and to see faults in them which he should see in himself. His distorted view is perpetuated and elaborated from one situation to another, and, due to a series of consistent misconceptions, he educates himself to an erroneous belief, a system of delusions. As his opinions become more and more out of harmony with his environments, so also his actions become disordered, and he reacts, not to his actual environment but to his distorted view of it. His interest and energy do not fade but they become restricted to the factors pertaining to his delusions, which absorb more and more of his attention. In some cases the patient maintains close contact with reality, and limits his imagination to creating false interpretations, affected by his prejudice, but otherwise logical. Such cases may come in the class of true paranoia. If, however, he allows his imagination freer play and accepts poorer judgments which are more obviously wrong, he will come in the class of paranoid schizophrenia. Although such patients do not become detached from reality they accept more imaginative ideas, their delusions are far fetched and perhaps extremely grandiose, and hallucinations are prone to develop. In all paranoid cases the individual's view of reality goes through a steady process of distortion based on illogical deductions, so that it is almost impossible for him to be re-educated to see the world normally. Moreover his view could only be corrected if his abiding prejudice could be overcome and this is almost impossible.

Therefore, the prognosis for recovery is bad. On the other hand, in as much as the minds of such persons do not become disorganized, and their interests and energy are fairly well maintained, there is less tendency to deterioration.

(c) *Example of paranoid type.*

(Case No. 5934 P.M.H.)—This man was 46 years old when admitted on December 6, 1932. There was no history of nervous or mental disease in his family. He was born in Scotland. His infancy and childhood were normal. After finishing the second year in high school he worked in an accountant's office for a while. In 1904 he came to Canada. As he did not like farming he soon obtained work in a bank. He was overseas from 1915 to 1919, during which time he contracted gonorrhœa. Returning to Canada he held several positions as a bank manager. Being dissatisfied with this he eventually became a life-insurance agent.

He was always very reserved, shy, and suspicious. He was ambitious and serious-minded. He was only slightly interested in women. "The feeling I have had about my infection has deterred me from seeking female associates". He had a history of diphtheria, pleurisy, trench fever and gonorrhœa. There were no previous mental illnesses.

Although his present illness became manifest rather suddenly, its etiology may be traced back through many years of misinterpretation of his environment. While in the bank before the war the patient repeatedly thought that he was not getting the promotion he deserved. In 1910 he "believed favouritism was being shown". His salary increases were small, yet he thought he did more than his share of work. "It took three junior men to replace me." He was suspicious of one of his seniors and had friction with him. "He did not see things as I did. I tried to keep things straight. He was not treating the bank the way he should have done." During his military career he qualified as a captain, but was never given an appointment. He felt his senior officers discriminated against him because he stood up for the men. When in the position of bank manager he clashed with an inspector. "He practically called me a liar about statements of fact. It was probably foolish of me to lose my temper. He reported that I had a peculiar disposition and was unfit to be a manager where there was competition." In the insurance business he was not as successful as he anticipated.

pated. He therefore developed the idea that his prospect list was being tampered with. He felt superior to his manager and was suspicious. He imagined the manager was afraid he would get his job.

About this time the patient imagined an old military companion was spreading the tale that he had syphilis. He thought others talked about him and that they shunned him. He believed they gave him dope to increase his sexual feelings. He became interested in a girl, thought he heard her voice, and became jealous of another friend of hers. When committed to hospital he thought he had been framed. Since then he has got steadily worse. He has been suspicious, fault-finding, uncooperative and abusive. He hears obscene voices and feels that he is being worked on with electric rays. His speech is coherent and there has been little deterioration.

#### CONCLUSION

Although these four psychologically distinct processes may be distinguished (diminution, disorganization, detachment, and distortion) and a few patients display them typically, one finds that most schizophrenics do not fit distinctly into any one group. This appears to be due to the fact that frequently several of these processes are going on in one individual with the result that the manifestations are mixed. Rather than to classify each case as belonging to one particular type of schizophrenia, it might be better to estimate which is the predominating process involved and what proportion of the other reactions may be present. Diagnosis would thus be interpretive rather than symptomatic, and the prognosis as to recovery, arrest, or deterioration, would be rational rather than categorical.

The writer wishes to express his thanks for the assistance of Dr. G. A. Davidson, Superintendent of the Provincial Mental Hospital, at Ponoka, Alberta, and his permission to refer to hospital cases.

#### AMPUTATION OF A LIMB UNDER LOCAL ANÆSTHESIA.

—L. Dambrin considers that general anaesthesia for the amputation of a limb is often followed by grave post-operative complications. The patient may be severely injured and in a state of shock, or suffering from an acute infection or gangrene, and the administration of general anaesthesia is liable to lead to complications in the liver, heart, or lung. Local anaesthesia is most satisfactory, and ensures an amputation without operative mortality or complications. A method is described by which complete anaesthesia of the arm can be obtained in three minutes and of the thigh in four minutes. The only case in which this form of anaesthesia is stated to be unsuitable is that of the amputation of the thigh of a fat woman. The method which has proved the most successful is the circular infiltration of the various layers of the limb, beginning with the skin, then the cellular

tissues, muscles, nerve trunks, down to the bone. A solution of 1 or 2 per cent novocain without adrenaline is injected after a tourniquet has been placed round the upper part of the limb. Three punctures are made in the arm and three or four in the leg, and the needle is rotated in each place. The amount of solution used is about 100 c.cm. for the arm and 150 c.cm. for the thigh. By this means perfect anaesthesia is obtained, and the amputation can be conducted without any risk of pain to the patient. In twenty cases reported there were no signs of intolerance to novocain, convalescence was uncomplicated, and there was no operative or post-operative death due to the anaesthetic. Since the series of cases included several patients suffering from diabetic gangrene or a virulent infection, it is pointed out that this would not have been the case had a general anaesthetic been given.—*Rev. de Chir.*, March, 1936, p. 245. Abs. in *Brit. M. J.*

## MUSSEL POISONING IN NOVA SCOTIA

BY ARTHUR L. MURPHY,

*Halifax, N.S.*

THE old warning, never to eat shell fish in months without an *r*, probably originated among the folk who live by the sea, and had no more scientific basis than the belief that good sauerkraut can be pickled only in the full of the moon. The superstition about the sauerkraut has been pretty well discarded by the younger generation in Nova Scotia, but those who enjoy the relish claim that it is not so good as it used to be. Disregard of the shell fish warning has resulted more seriously. There have been two fatalities, attributed to the eating of mussels.

On July 7, 1936, at 1 p.m., Dr. F. E. Rice, of Sandy Cove, Digby County, was called to Centreville, some five miles distant, to a sick boy. Responding immediately he found a well developed boy of eight years, deeply unconscious. His colour was very pale; he was pulseless. The heart could just be heard, being very rapid and weak. Within ten minutes he was dead.

The patient, with another boy of his own age, had gone to the shore in the morning to gather mussels. Centreville is on St. Mary's Bay, an inlet of the Bay of Fundy, and the blue-black shell fish are to be found in abundance on the mud flats when the great Fundy tide has swept out. At about 10 a.m. they cooked the mussels over a fire and ate an undetermined number. Shortly after, feeling ill, they went their own ways home. The patient vomited persistently and complained of faintness, but it was not until this merged into coma that his father became alarmed and called the doctor. The boy's companion, after a bout of vomiting and vertigo, made a rapid recovery.

At 1.30 p.m., the same day, Dr. Rice was called to East Ferry, fifteen miles from Centreville. He found two men faint and vomiting. They complained of numbness in their hands. Lying on the floor was a third, deeply comatose, moribund. His pulse was 160; his hands were pressed against his abdomen. In fifteen minutes, two hours and a half after eating mussels, he died. His companions quickly recovered. They had eaten only a few mussels, both cooked and

raw, whereas the victim had taken a considerable number. Dr. Rice regretted that the rapid termination of both cases made a more complete clinical picture impossible.

Shell fish poisoning has been recognized as a clinical entity for over a century in Europe where it was first described and the literature records 120 cases with 24 deaths. Outbreaks in California during the past nine years have produced 240 cases with 14 deaths and the only thorough work done on the problem comes from the University of California. Hermann Sommer and Karl F. Meyer of the George Williams Hooper Foundation have done extensive research (*Calif. & West. Med.*, 1935, **42**: 423) and, while the exact nature of the poison has not been determined, valuable facts have been established.

The poison is most common in the mussel but has been found in the clam and sand crab. Guinea pigs fed on a species of clam gathered on the Bay of Fundy shore in the regions of Centreville and East Ferry died in forty-five minutes. Their brethren, fed on mussels from the same areas, died after a longer interval. Like the human beings, some of the guinea pigs escaped after a slight illness or none at all. Beyond confirming the presence of the poison no experimental work was done at the provincial laboratory at Halifax, specimens being shipped to Dr. Meyer in California. Nevertheless a few observations may be drawn from the local cases which conform with the established findings.

First, the poisoning takes a paralytic form. Although no information could be elicited from the fatal cases the two men who recovered complained of numbness in the hands. This may extend from the four extremities until the whole body is paralyzed. The poison is quickly eliminated; the recoveries of those who escaped death were rapid. It is present in fresh mussels. It is not present in lethal quantities in all the mussels of a particular region, nor are the mussels of any region always poisonous. Many have eaten of St. Mary's Bay shell fish without ill effect. The poison is not from contaminated

water. The Bay is too exposed to the Atlantic, its shores too sparsely settled, to make this tenable. The poison is not destroyed by boiling or cooking, or the boy would not have died. From the rapidity of its action it is not likely bacterial, and cultures made from different parts of the mussels confirm this.

Meyer and his co-workers, gathering mussels near San Francisco over a seven year period, and determining the degree of toxicity by the intraperitoneal injection of mice, have shown the almost constant presence of poison. This is highest in the summer months, from June to September. In some years this peak transcends the lethal danger line, in others it does not. The occurrence of poisoning cases has been found to coincide with these results.

Mussels gathered at the lowest possible level are more poisonous than those exposed to the sun or those gathered in placid, land-locked bays. This suggests that the source of the poison may be in the sea, possibly the plankton on which the mussel feeds. Experiments in this direction have not been conclusive.

The poison is a basic alkaloid. The purest preparations so far obtained are lethal to mice in doses approaching one-millionth of a gram on intra-peritoneal injection. Thus it may be present in sufficient amount to kill without outward warning of its existence. It is one of the most active known chemical poisons. Only the antigenic toxins of some plants and bacteria are more potent. It is present in the digestive gland and the fluid about the fish. The muscle is probably unaffected.

The toxic molluse has no distinguishing feature, although, usually, it has a fuller intestinal tract and larger digestive glands than its normal mate. There is no known antidote to the poison. Eighty per cent may be neutralized by boiling in soda bicarbonate solution for twenty minutes. Here, unfortunately, cook and toxicologist disagree. Education of the people would seem to be the only safeguard, and they have been warned not to eat mussels in the months without *r*, September and October being added, if only to show that science really is greater than superstition.

#### CARBON TETRACHLORIDE POISONING\*

By CECIL YOUNG, B.A., M.B.(TOR.), M.R.C.P.(LOND.),

Toronto

CARBON tetrachloride, used as a solvent for fats and oils, has been in common use in industry and in the home for many years. The safety element has been stressed, because it is non-inflammable as compared with gasoline and similar dry-cleaning preparations. Carbon tetrachloride is also an ingredient of "Pyrene" or similar hand fire extinguishers in common use in buildings, yachts and motor cars. As a vermifuge it has been used internally in the treatment of hookworm disease.

Recently it has been noted by many observers that carbon tetrachloride is not without danger if the fumes are inhaled in concentration. Butsch<sup>1</sup> reported poisoning in a workman who used carbon tetrachloride in cleaning old telephones. McGuire<sup>2</sup> reports seven cases of poisoning in employees of a dry-cleaning establishment where carbon tetrachloride was used. Alice

Hamilton<sup>3</sup> notes the danger of carbon tetrachloride as a fire extinguisher in the presence of heat in a closed space, under which conditions phosgene is generated. The *New York Times*, July 7, 1932, reported a fire in a New York subway in which "Pyrene" fire extinguishers were used and 150 persons were overcome with the fumes, which were probably a mixture of carbon tetrachloride, phosgene, and chlorine. The *Journal of the American Medical Association*,<sup>4</sup> in an editorial on the subject, states that in Portsmouth Navy Yard in 1919 two men died from the fumes produced when the clothing of one caught fire and Pyrene was used to extinguish the flames. The same editorial also reports poisoning from carbon tetrachloride used in Switzerland as a solvent for floor wax.

McMahon and Weiss<sup>5</sup> were of the opinion that an individual's susceptibility played an important part in tetrachloride poisoning, and also stated that patients who were accustomed to the

\* Read before the Section of Medicine, Academy of Medicine, Toronto, February 11, 1936.

regular consumption of alcohol were particularly susceptible. They concluded that the sensitivity was increased not only because of the increased absorption of the drug and the synergistic action of the alcohol and carbon tetrachloride but also because of the possible existence of pre-existing liver damage in alcoholics.

The majority of cases reported have shown liver damage due to central necrosis, and a few cases have been reported as exhibiting kidney damage, including that of Lehnher<sup>6</sup> who made a very complete study of the blood chemical changes on an alcoholic patient who drank four or five ounces of carbon tetrachloride. The case I am about to report differs slightly in that the patient was practically a total abstainer from alcoholic drinks, and received practically no liver damage but severe kidney damage, the latter to such an extent that on noticing the blood chemistry figures one is gratified at the remarkable and steady improvement following intravenous therapy.

#### CASE REPORT

Mr. H. B., aged 42, married, embalmer, was admitted to the Toronto Western Hospital on October 29, 1935. He stated that he had been in good health until ten days previously, when he had carried out an extensive fumigation, lasting two hours, in a small room with the doors and windows closed, by spraying walls, floor and baseboards with a liquid obtained from a neighbour who worked for a fire extinguisher manufacturing company. The substance was found to be carbon tetrachloride. That evening, about an hour after he finished fumigating, he experienced cramps in the upper abdomen, with extreme fatigue, nausea and vomiting. The nausea and vomiting had continued at intervals up to the time of admission, with obstinate constipation, and during the past two or three days he had passed very little urine and his vision had begun to blur. He mentioned that his wife and two children had felt nauseated the evening of the fumigation, but had felt perfectly well since.

*Personal history.*—He had had rheumatic fever; tonsillectomy three years ago. He was a moderate smoker and practically an abstainer from alcohol.

*Family history.*—Irrelevant.

*Physical examination.*—The man appeared ill; his expression was strained and pallor marked. His pupils were equal and reacted to light and accommodation; ocular fundi normal. Some blurring of vision was noted. Hearing was normal. Post-nasal discharge; tongue heavily coated; lower teeth, carious. There was no enlargement of cervical or other glands. The thyroid was not enlarged.

*Cardiovascular system.*—Pulse 85; no radial sclerosis. Blood pressure, 160/84. The heart was slightly enlarged (apex 9.5 cm. to left, in fifth space). Heart sounds clear and of good quality.

*Lungs.*—Normal.

*Abdomen.*—Some vague tenderness in right upper quadrant and posteriorly over right costo-vertebral angle.

*Nervous system.*—Involuntary twitching of hands. The tendon reflexes were all a trifle exaggerated. Babinski and Kernig signs were not elicited.

*Urinalysis.*—Urine, alkaline; specific gravity, 1.017; albumin, 2 plus; sugar, negative. Microscopically, red

blood cells, 30-60; white blood cells, 200-250; a few granular casts; mucus, 2 plus.

*Blood count.*—Red blood cells, 4,700,000; white blood cells, 9,300; haemoglobin, 70 per cent. Differential count.—Neutrophiles, 72 per cent; eosinophiles, 2 per cent; lymphocytes, 23 per cent; monocytes, 1 per cent.

*Blood Wassermann test.*—Negative.

*Blood chemistry.*—Non-protein nitrogen, 203 mg. per 100 c.c.; creatinine, 22.7 mg. per 100 c.c.; van den Bergh, very slightly biphasic; icterus index, 9.

*Blood culture.*—No growth.

*Blood grouping.*—Type 1 Jansky.

November 6, 1935, galactose tolerance test.—40 g. galactose.

Hour	Quantity	Galactose
Fasting urine	150 c.c.	negative
2 hour	138 c.c.	very strong trace
5 "	225 c.c.	negative

*Diagnosis.*—Carbon tetrachloride poisoning; acute nephritis and uremia.

*Treatment.*—Intravenous glucose, 25 per cent, 300 c.c., was given twice a day; calcium gluconate, 10 per cent, 10 c.c. intravenously, twice a day. Diet: fruit juices and glucose drinks only.

*Progress.*—The patient commenced to improve at once after the use of intravenous glucose and did not vomit after the third day, but on the fifth day an exsanguination transfusion was done, removing 800 c.c. of blood and replacing it with 500 c.c. of donor's blood with the addition of 1,000 c.c. of 5 per cent glucose. This apparently was of great benefit to him. On the seventh day his diet was changed to one consisting of banana, 900 g.; cream, 200 c.c.; cream soup, 200 c.c.; milk, 200 c.c.; and cocoa, 200 c.c., giving him a value of 1,585 calories and a protein content of 35.4 g. By the ninth day the urine had improved so that there was only a slight trace of albumin, and microscopic examination showed only an occasional pus cell with no red blood cells or casts, although from the amount of glucose given intravenously he showed an occasional trace of sugar. The level of non-protein nitrogen and creatinine in the blood showed a steady decline, and his blurring of vision had cleared by the sixth day. At no time did he show any further evidence of hepatic derangement other than a faintly indirect van den Bergh reaction and an icterus index of 9. He made an uninterrupted recovery. The blood chemistry figures are interesting.

Date	Non-protein nitrogen in mg. per 100 c.c.	Creatinine in mg per 100 c.c.	Diet
Oct. 31st	203 .....	22.7	
Nov. 1st	207		Fruit juices and glucose.
Nov. 3rd	203		
Nov. 4th	179		
Nov. 5th	160		Nov. 6th
Nov. 6th	140		Protein, 35.4 g.
Nov. 7th	112 .....	8.9	Calories, 1,585.
Nov. 8th	98		
Nov. 9th	77		
Nov. 10th	72		
Nov. 11th	63		
Nov. 12th	54		
Nov. 14th	56 .....	2.6	Nov. 15th
Nov. 15th	46		C.300 P.30 F.40
Nov. 20th	42		Calories, 1,680.
Nov. 21st	39		
Nov. 23rd	35		
Nov. 27th	35 .....	1.7	Intravenous glu-
Dec. 8th (after 26 discharge)			ucose and calcium discontinued.

## COMMENT

This case illustrates the profound and rapid toxic effect of the inhalation of carbon tetrachloride fumes on the kidney, and also illustrates the value of glucose and calcium intravenously in this condition. The subjective symptoms improved dramatically after the exsanguination transfusion, and I believe this to be a useful procedure in such cases. For the use of calcium we are indebted to Minot and Cutler<sup>7</sup> who found that dogs poisoned with carbon tetrachloride could be treated with injections of calcium, also

that with a high calcium diet dogs were relatively immune.

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## OBSERVATIONS ON THE INTESTINAL FLORA FOUND IN MONTREAL

By PAULINE BEREGOFF-GILLOW, Ph.G., N.S., M.D.,\*

*Montreal*

OWING to the uncertainty prevailing regarding the distribution and significance of parasites and pathogenic bacteria of the intestinal tract, and due to the general lack of knowledge about the etiology of certain intestinal diseases, the slightest observations may have some degree of value in promoting further research. I present, therefore, some data on the intestinal flora, both bacterial and parasitic, which I have obtained from a study of 400 cases.<sup>†</sup>

## MATERIAL

Repeated specimens of faeces were examined from the following persons (in the majority of cases as many as 10 to 12 specimens):—

Children . . . . .	200	Hospitalized for different causes (heart, lungs, tonsils, etc.).
	25	With history of gastrointestinal upsets (diarrhoea, cramps).
Infants . . . . .	3	Acute enteritis.
Adults . . . . .	80	Ward patients with no apparent gastrointestinal disturbances.
	8	Ward patients with gastrointestinal upsets (diarrhoea).
	4	Ward patients; typhoid cases.
	25	Referred private patients with history of repeated diarrhoeas.
	55	Controls, from among the hospital staff (doctors, nurses, maids, etc.).

## TECHNIQUE

All the specimens were obtained in as fresh a condition as possible, and examined as follows:

## 1. Grossly—for adult worms.

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†The majority of cases were from the Women's General Hospital; several from the Montreal General Western Division; and 18 from the Montreal Children's Hospital.

2. Fresh cover-glass preparations—for ova, larvæ, amœbæ, etc.

3. Sediments—Rivas' concentration method<sup>1</sup>—for parasites, encysted amœbæ, etc.

4. Cultures—Each specimen was plated directly on Endo and McConkey media. Those colonies differing from the *B. coli* type were transferred to standard agar plates and Russel stabs. If the cultures appeared pure after 24 to 48 hours' growth several colonies were then transferred to agar tubes and subsequently inoculated into dextrose, lactose, saccharose, peptone, gelatine, maltose and mannite broths, etc., for preliminary identification. Mixed cultures were separated by plating. All strains that seemed to show any characteristics of the paratyphoid, typho-dysentery, and Morgan groups were kept for further study. The majority of the strains transplanted and then discarded were those of the proteus type, *B. alkaligenes*, and those that slowly ferment lactose.

## RESULTS

## 1. Intestinal parasites isolated:

## METAZOA

Cestoda—	Adults	Children
<i>Dibothriocephalus latus</i> . . . . .	2	1
<i>Taenia solium</i> . . . . .	1	0
<i>Taenia saginata</i> . . . . .	0	1
Nematoda—		
<i>Oxyurus vermicularis</i> . . . . .	0	21
<i>Trichocephalus</i> . . . . .	3	10
<i>Ascaris Lumbricoides</i> . . . . .	3	8

PROTOZOA			<i>B. sonne</i> .....	0	2	
		Adult	Children			
Sarcodina—						
<i>Entamoeba histolytica</i> .....		12	0			
<i>Entamoeba coli</i> .....		15	20			
<i>Entamoeba nana</i> .....		5	7			
Mastigophora—						
<i>Giardia intestinalis</i> .....		5	20			
<i>Cercomonas hominis</i> .....		2	4			
<i>Trichomonas intestinalis</i> .....		2	7			
Ciliata—						
<i>Balantidium coli</i> .....		1	0			
Eleven of the children were infested with 2 or 3 species of parasites.						
2. Bacterial pathogens isolated:—						
	Adults	Children				
<i>B. typhosus</i> ...	6	0	Of these, two were carriers. In one of the stools of a typhoid patient <i>E. histolytica</i> was also found.			
<i>B. para-typhosus "A"</i>	10	0	Isolated from 5 cases of mild hyperexia with slight diarrhoea; from one attendant, considered the carrier, and from other 4 members of the staff who had no symptoms whatever.			
<i>B. para-typhosus "B"</i>	4	0	These patients presented no gastrointestinal disturbances.			
<i>B. aertrycke</i> ...	3	0	These patients suffered from occasional diarrhea, alternating with constipation. This organism isolated fermented dextrose, maltose, xylose, sorbitol, arabinose, dulcitol and trehalose. It produced H <sub>2</sub> S, no indol, did not liquefy gelatine, and did not ferment salicin, lactose or saccharose.			
<i>B. flexneri</i> ....	2	0	Normal persons.			
<i>B. morgani</i> ...	2	3	The children had frequent attacks of diarrhea; the adults, acute diarrhea. Because of the fact that repeated examinations showed no other pathogens, and because the Morgan organism was constantly present, almost in pure culture, it is reasonable to believe that this organism was the etiological factor.			

## DISCUSSION

These observations indicate that systematic stool examinations would clear up a considerable number of unrecognized bacillary and parasitic intestinal infections which are the cause of, or may eventually lead to, gastrointestinal disturbances. They also stress the relative importance of recognizing the sources of these pathogens.

It is interesting to note that the children in these regions are harbouring the same type of flora as those of the tropics. Though there is a smaller percentage of infestations, the variety of the species is practically the same. Although we are inclined to believe that in these regions we are free from parasitic infestation and that our hygienic conditions tend to eliminate bacterial pathogens, I would, nevertheless, stress the desirability of an intensive study of the various types of gastroenteritis. I feel that a routine stool examination should have been generally adopted long before now, as is done in the tropics.

The epidemiological relation and the distribution of the types of bacterial and parasitic infestation deserve greater investigation, and more appropriate preventative measures should be taken.

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## Case Reports

### A CASE OF ANURIA LASTING TEN DAYS ASSOCIATED WITH MARKED TOXIC SYMPTOMS\*

By A. S. SINCLAIR, M.D.,  
*Regina, Sask.*

It is my purpose to present a case of anuria which lasted ten days and was followed by complete recovery. The anuria was preceded by partial urinary suppression for two days. Both the suppression and anuria followed a haemolytic blood transfusion given to a patient subject to acute influenzal infection complicated by severe gastric haemorrhage. The anuria was accompanied by marked symptoms of intolerance to the unexcreted poisonous nitrogenous substances in the blood stream. This patient had a solitary kidney; the other one was tuberculous and was removed in 1932.

During the period of anuria the following features were observed. (1) The blood clotted very rapidly. (2) The fragility of the erythrocytes was unusually increased. (3) The skin and subcutaneous tissue of the whole of the abdominal wall were riddled with deep-seated and extensive purulent lesions. These lesions resembled carbuncles. (4) The blood donor and recipient were cross-typed and said to be entirely compatible, and yet the transfusion was followed by delayed reaction.

#### CASE REPORT

The patient was a female, aged 32, with a history of catarrh of the upper respiratory tract, sneezing, and a non-productive hard cough, for 14 days. She had headache and epigastric pain for seven days, and a moderate fever for one or two days. The pain in the head, eyeballs and back was intense. Her vision was blurred and she complained of flashes of light in front of her eyes. She had vomited several times. The pain in her left lumbar region was particularly noticeable on the day of her admittance to the hospital, October 28, 1932. She also complained of some slight burning during micturition, shortness of breath, feeling of weakness and loss of appetite. Her bowels were regular and there was no frequency of urination.

*Past history.*—Appendectomy in April, 1930. Dilatation and curettage, followed by blood transfusion in November, 1930. The haemorrhage was caused by an abortion of a four months' pregnancy. In December, 1931, she was confined to the Regina General Hospital for toxæmia of pregnancy. She was under my care and made an uneventful recovery. Later her condition was

found to be a right cornuate pregnancy and she aborted in March, 1932.

Nephrectomy was performed by Dr. Dakin and myself in April, 1932. We removed her right kidney which was practically destroyed by tuberculous infection. She was sent to the Fort Qu'Appelle Sanitarium for a rest cure for two and one-half months. She had been enjoying comparatively good health until her present illness set in. The family history was irrelevant.

*Physical examination.*—On admission the patient was toxic but ambulatory. She was thin, pale, and sickly looking. Her skin was dry, her pupils were sluggish, her conjunctivæ were injected, and photophobia was present. Her temperature was 104° F.; the pulse rate 98; respiratory rate 20; and the blood pressure 115/80. The lungs were negative except for some dullness at the bases on percussion. The apex of the heart was localized in the nipple line and there was a mitral systolic murmur. The pulse was dicrotic and somewhat irregular in character. There was definite tenderness and splinting in the epigastric region and over the left kidney region. The spleen was not palpable. The deep reflexes were sluggish. The remainder of the physical examination was essentially negative at this time.

*Laboratory tests.*—Red blood corpuscles, 3,328,000; white blood cells, 6,000; haemoglobin, 68 per cent; colour index, 1. Urinalysis—urine was cloudy, of amber colour, acid reaction; specific gravity was 1.026; a faint trace of albumin; no sugar or acetone was present; an occasional pus cell and hyaline cast. The blood urea nitrogen was 28 mg. per 100 c.c. The blood creatinine was 1.2 mg. per 100 c.c.

*Course.*—October 27th to November 9th.—Septic temperature; severe headache, pain in chest and abdomen; face flushed and hot; drowsy; feeling chilly at times; slight epistaxis (once or twice), nauseated, belching up gas and vomiting undigested food.

October 31st.—No tubercle bacilli or pus found in urine.

November 14th to 19th.—Gradual rise in temperature, reached 104° F. on November 19th at 3 p.m. The same day she had a chill which lasted 20 minutes, and vomited. Face was flushed; eyes puffy, photophobia present; appetite is fair. Headache; complained of whistling sound in head; became very drowsy after the chill. Blood urea was estimated and reported to be 28 mg. per 100 c.c. Urinalysis, negative.

November 19.—X-ray of left kidney—left kidney outlined, inferior pole opposite the third lumbar vertebrae. Kidney fairly low, slightly enlarged, no evidence of irregularity; psoas muscles normal; diaphragm normal.

November 20th to 24th.—Very drowsy, complaining of chilliness, vomiting, and perspiring freely. Slightly irrational.

November 24th.—Expelled 5 oz. of very dark red blood containing clots by bowel; the odour was very offensive.

November 25th.—Expelled 2½ oz. of very dark red blood containing clots; very offensive odour; patient very restless and pale.

November 26th.—Stool contained about 4 oz. dark red blood; involuntary micturition, very pale and restless; gave blood transfusion of 350 c.c. No immediate reaction. Two hours after arrival in ward developed chill lasting for 20 minutes. Stool contained 5 oz. dark clotted blood. Another bowel movement contained 2 oz. dark blood; patient appears tired and very pale, intake 32 oz., output 28 oz.

November 27th.—Pale, restless, vomiting, facial pallor pronounced, temperature subnormal, drowsy; gave intravenous saline; intake 22 oz., output 10 oz.; first indication of suppression of urine.

\* Read before the Grey Nuns Medical Staff, Regina, May 28, 1936.

November 28th.—Appears brighter, temperature normal, no blood in stool, intake 33 oz., output  $1\frac{1}{2}$  oz. Blood clotted with unusual rapidity. Fragility of erythrocytes was unusually increased.

November 29th.—Passed  $\frac{1}{2}$  oz. of urine; very drowsy and restless. Cystoscopic examination by Dr. Dakin; bladder and ureteral opening normal; no obstruction to catheter; kidney irrigated with warm saline. Dr. Dakin obtained  $\frac{1}{2}$  dram of urine from kidney and laboratory report was as follows: "From left kidney micro: few red cells (1/3 h.p.f.), small round epithelial cells." X-ray of chest was taken. Heart is enlarged in the aortic and basal areas. Heart is centrally placed; enlargement is towards the right. Apices are clear. The film taken is a little light, showing rather intense lung markings with an indication of some mottling of the right chest, and passive congestion in the lower half of both right and left chest. One could judge from the appearance of the film that there is cardiac insufficiency producing basal lung stasis."

November 30th.—No urine passed; very restless, irrational, attempted to get out of bed, unable to obtain urine after catheterization; hands and feet trembling, vomiting.

December 1st.—Considerable twitching of limbs; lips very dry; very restless; hands cyanosed; unable to count pulse; spent a poor day.

December 2nd.—No urine obtained from bladder, several bowel movements, blood urea 220 mg. per 100 c.c. Creatinine 5.36 mg. per 100 c.c.

December 3rd to 8th.—Has not voided, developed deep skin sores all over her abdomen; very restless, trembling, mumbling. Nauseated; appears to have pain when she turns. Blood urea 260 mg.; creatinine 5.8 mg. per 100 c.c.

December 6th.—Hæmoglobin, 30 per cent; red cells, 1,880,000; colour index, 0.8. Differential count: white cells, 100; polymorphonuclears, 67; small lymphocytes, 33.

December 9th.—Frequent emesis of dark green fluid with bloody mucus. At 10 a.m. examination revealed distended bladder; catheterized and obtained 19 oz. of urine.

December 10th.—Brighter; voided 22 oz. Pustules on abdomen becoming larger.

December 11th.—Urine culture and examination for tubercle bacillus culture (after 11, 35, 48 hours) shows a pure culture of streptococcus; smear examination for tubercle bacillus was negative.

December 14th.—Blood urea, 296 mg. per 100 c.c.

December 24th.—Blood urea, 24 mg. per 100 c.c.

December 19th.—Phenolsulphonephthalein dye injected intramuscularly.

1st specimen....1.10 hour after injection 13 per cent  
(normal 40 to 50 per cent)

2nd specimen....2.10 hour after injection 10 per cent  
(normal 20 to 25 per cent)

24 to 11 per cent indicated renal function markedly impaired.

January 17th.—Phenolsulphonephthalein test.

1st specimen....15 minutes after injection 10 per cent  
2nd specimen....30 minutes after injection 15 per cent  
3rd specimen....60 minutes after injection 15 per cent

Total elimination of the dye.....40 per cent

59 to 40 per cent renal function slightly impaired.

January 29th.—The dye was injected intravenously.

1st specimen....15 minutes after injection 11 per cent  
2nd specimen....30 minutes after injection 12 per cent  
3rd specimen....60 minutes after injection 16 per cent  
Total elimination of dye.....39 per cent

39 to 25 per cent is interpreted as renal function moderately impaired.

February 10th.—Report of gastro-intestinal tract. Stomach shows some spasm at pylorus; cap forms

normally on films; colon shows delay in emptying; evidence of slow motility, otherwise series is negative.

Urine: cloudy yellow, reaction acid; specific gravity 1.008; albumin negative; sugar negative; acetone negative; few leukocytes, epithelial cells.

February 11th.—Hæmoglobin, 63 per cent; red cells, 3,190,000; colour index, 1.0; white cells, 8,000; coagulation time,  $3\frac{1}{2}$  minutes.

February 17th.—Colour, clear yellow; reaction, neutral; specific gravity, 1.016; albumin, negative; sugar, negative; acetone, negative; epithelial cells, microscopical.

December 24th to February 17th.—Slow uneventful recovery; temperature ranged between 97 and 104° F.; pulse ranged between 80 and 100, excepting during chills, when it rose to 118. Respiration ranged between 20 and 40 per minute. Blood pressure ranged from 88/52 to 106/70.

*Diagnosis.*—Influenza associated with gastric haemorrhage, nervous and renal involvement followed by anuria after blood transfusion.

#### TREATMENT

Treatment must be by prophylactic methods, as little can be done, once suppression of urine has developed. The use of high titre sera will tend to eliminate errors in grouping, while administration of fluids and alkalies before transfusion will ensure an alkaline diuresis, so that any haemolyzed blood will be excreted in solution. The following suggestions may be of value. (1) Hot applications or dry heat over kidney region. (2) Large amounts of fluids by proctoclysis or hypodermoclysis. The addition of alkalis 2 per cent and of glucose 5 to 10 per cent. (3) Salt solution should never be used. (4) Decapsulation is of little value. (5) Venesection preceded by intravenous saline has been suggested if convulsions threaten. (6) Hot baths or sweats if cardiac condition permits.

#### COMMENT

Although the blood donor and recipient were cross-typed and said to be entirely compatible this patient developed a *delayed blood transfusion reaction*, confirming the idea that the agglutinin content of some donors' blood sera may be so surprisingly high, namely, 1:200 instead of the usual 1:3, that serious results may ensue unless high titre sera are used when cross-typing the blood before transfusion.

On November 28th, when the laboratory technician obtained a specimen for a blood urea test he found that the blood clotted very rapidly. It would clot as soon as it was collected. This phenomenon was checked by Dr. Hookings, Laboratory Director, and he stated that not only was the clotting time unusually reduced but the fragility of the erythrocytes was unusually increased as well.

Two days after suppression set in this woman developed extensive and deeply-seated sores all over her abdomen. They were similar to multiple carbuncles of the skin. Over six weeks passed after the urinary secretion returned to normal before these cleared up. At present her abdomen is covered with irregular, healed scars.

In reviewing the literature, I have failed to find a case in which a patient with a solitary kidney and developing anuria with marked symptoms of intolerance to the poisonous nitrogenous substances for 12 days had survived. This patient recovered completely. Her kidney is functioning as well as it did prior to this illness. Her last urinalysis was done at my office a week ago and found normal.

One might venture to explain the recovery thus. Under normal conditions waste products are excreted by kidneys, liver, lungs, intestines and skin. The kidneys are of first importance. When they are unable to function the task may be assumed by the other excretory bodies. If the other excretory organs must do this work on short notice, as occurs in anuria, they fail to respond sufficiently to maintain life, because they have not been accustomed to act as substitutes. The reason this woman recovered may be due to the fact that she had a solitary kidney and the other excretory organs may have learned to substitute sufficiently to maintain life until the crisis subsided.

#### CONGENITAL ABSENCE OF THE CERVIX UTERI COMPLICATING PREGNANCY

By D. W. DAVIS AND J. F. HASZARD,

*Kimberley, B.C.*

A primipara, aged 26, first examined and diagnosed by Dr. W. Leonard, of Trail, B.C., was referred to us on her husband's transfer to Kimberley in September, 1935.

Heart, lungs and pelvic measurements were normal. There had been no previous operation, except for appendicitis. Pelvic examination revealed a shortened vagina and complete absence of the cervix uteri. The external os was very small.

It was decided to give her a test of labour before attempting more radical measures. Labour began about six p.m. on February 15, 1936, with intermittent light pains. Rectal ex-

amination at nine p.m. showed the head well advanced and no dilatation. At two-thirty a.m., February 16th, the pains became more severe and almost continuous. At four a.m. examination showed that the head was almost on the perineum with no sign of dilatation. As the os was obviously not going to dilate and we feared a rupture of the uterus, a Cæsarean section was done. With no cervix, a low Cæsarean was out of the question and the classical operation the only method possible. The further course of the case was uneventful, drainage through the small os being sufficient to allow a normal lochial discharge.

#### TWO CASES OF DIPHTHERIA OF THE CONJUNCTIVA\*

BY S. HANFORD MCKEE, B.A., M.D.,  
*Montreal*

Fuchs distinguishes two forms of conjunctival diphtheria, namely, the superficial or croupous, and the deep (diphtheria of the conjunctiva in the narrower sense). The croupous form is characterized by the presence of a greyish white membrane which adheres closely to the surface of the conjunctiva, but which can usually be removed from it easily. The deep form runs a much more serious course than does the superficial, as in order for it to occur the exudate must coagulate while still within the tissues of the conjunctiva, so that the vessels are compressed and necrosis consequently occurs. The two forms described, which differ considerably in appearance and course, are due to the same cause, the Klebs-Loeffler bacillus. Often patients present other diphtherial patches, such as of the nostrils, angles of the mouth, or there may be a fully developed nasal or pharyngeal diphtheria.

##### CASE 1

L.O.N., a female of 9 years, had been in her usual good health until October 12th, 1934, when she fainted. She was put to bed and remained there the following day, as she complained of a general feeling of malaise. Her mother noticed that her left eye was red, but allowed the child to return to school the following day. She was brought to the eye clinic on October 19th. The left eye at this time showed a definite conjunctivitis, the lids were swollen, and over the palpebral conjunctiva of both lids a thin greyish membrane was seen, which could be removed by the platinum wire without bleeding. The membrane reformed rapidly, while a slide was being prepared for examination.

\*From Departments of Ophthalmology and Pathology, Montreal General Hospital.

Read before the American Ophthalmological Society, Hot Springs, Va., on June 1st, 1936.

Examination of the smear showed micro-organisms morphologically similar to the diphtheria bacillus. Cultures were then made on Loeffler's blood serum, and organisms again morphologically similar to the diphtheria bacillus were found. The patient was transferred to the Alexandra Hospital for Contagious Diseases with a diagnosis of diphtherial conjunctivitis. During the course of her examination she had been taken to the Nose and Throat Department where examination showed no other evidence of diphtheria. The culture obtained was sent to the Department of Bacteriology of the McGill Medical School, and the report from Dr. F. Smith is as follows:—

"With regard to the micro-organisms in your case of diphtheritic conjunctivitis, I injected a guinea pig with the culture as it was received. There resulted only a slight local induration during the first few days. Metachromatic granules were not a prominent feature of the organism, and its fermentation reactions did not conform to those accepted for the diphtheria bacillus, so that my provisional report was that the organism resembled the Xerosis bacillus. On the fourth day the guinea pig died without any obvious lesion, and I repeated the virulence test with a larger dose of a young culture, giving a control pig 500 units of antitoxin. The pig died within 24 hours, a typical diphtheria death (local haemorrhagic edema and haemorrhagic suprarenals). After two days the control pig is perfectly well. Morphologically and biochemically, the organism would be missed, but there is no escaping the second guinea pig test. This is a diphtheria bacillus. It would be interesting to test its ability to produce toxin. I should not think that this is very high."

The patient received antitoxin treatment at the Alexandra Hospital, and was seen by me three days after her admission. Her eye had quieted very perceptibly and no sign of membrane was present. She made an uninterrupted recovery, and later (November 9th) was seen by me at the Montreal General Hospital, where the eye was found to be quite normal in every way.

#### CASE 2

M.D., a boy of 5 years, was brought to the Montreal General Hospital on May 27th, 1935, and when examined was found to have a well-marked membranous conjunctivitis of the right eye. Examination showed numerous organisms corresponding in morphology to the bacillus of diphtheria. A piece of the membrane was removed from the eye and sent to the Pathological Laboratory for investigation. Small fragments of the membrane were teased out upon slides and stained with old alkaline methylene blue and Albert's stain for *B. diphtheriae*. In the specimen numerous polymorphonuclear leucocytes and numerous straight and curved bacilli were seen. A good many of the bacilli showed clubbed ends and some of them segmentation. A specimen of the membrane stained with Albert's stain showed that the bacilli contained varying numbers of intracellular deeply staining granules. A series of tubes containing Loeffler's blood serum were inoculated with the membrane. There developed in the tubes over night one colony of *Staph. albus* and many colonies which contained in pure culture an organism which showed the characteristic morphology

and staining reaction of *B. diphtheriae*. After 40 hours' growth these colonies had increased in size, were sharply outlined, smooth and glistening, had a raised curve, and showed the typical poached-egg appearance of *B. diphtheriae*. When stained with old alkaline methylene blue and Albert's stain the organisms of which these colonies were composed showed the morphology and staining characteristics of *B. diphtheriae*. A typical colony planted in selected sugar serum waters gave the following reactions: Dextrose acid and no gas on dextrose, maltose and dextrin; no acid and no gas on saccharose, lactose and mannite.

Cultures of the diphtheria bacilli isolated, planted on Morgan's media (tellurite), showed black, discrete, shiny colonies with a grey margin.

In carrying out the virulence test, two guinea pigs of 240 gms. weight were used. On the day before inoculation one was given 500 units of anti-diphtheritic serum (Lederle). The following morning each pig was given 1.c.c. of an 18-hour growth of a pure culture of the organism isolated from the membrane of the conjunctiva. The protected pig was not ill. The unprotected pig died within 36 hours, and showed a local hemorrhagic exudate at the site of inoculation, general congestion of the viscera, and haemorrhage in the adrenals. An organism was isolated from the site of inoculation of the unprotected pig which was in every way similar to the diphtheria bacillus that had been subcutaneously injected. The above procedure was carried out three times, each time with the same results. The degree of virulence was very high.

A pig inoculated intraperitoneally with the water of condensation and surface contents of a 24-hour culture died within 6 hours from soluble toxins present. Some of the material from the same tube as that injected into the guinea pig was washed in salt solution and centrifuged, and the supernatant fluid decanted. The precipitate was again washed and reprecipitated. Dilutions of these washed organisms when injected into an unprotected guinea pig killed the pig after 48 hours. The bacteriological diagnosis was a diphtheria bacillus of high virulence.

#### SUMMARY

Two cases of primary diphtheria of the conjunctiva are reported in a girl of 9 and a boy of 5 years. In Case 1, both morphologically and biochemically, the micro-organism was not typical; the guinea-pig test however left no doubt in the matter. The virulence of the micro-organism in Case 1 was mild, while in Case 2, the degree of virulence was high. In both cases examination failed to reveal diphtheria of any other part.

I wish to record my thanks to Dr. F. Smith and Dr. L. J. Rhea for their reports.

**CYCLOPROPANE ANÆSTHESIA.**—H. Killian discusses the chemistry, physics, and pharmacology of cyclopropane and reviews the accounts which have been published of this anæsthetic from Canadian and other sources. With the aid of a supply of the gas sent from America he has carried out animal investigations, self-administration, and a small number of surgical anæsthesias. His findings in the main support those of other observers — namely, that cyclopropane is a powerful

anæsthetic which must be used with due care, but that it is safe owing to the high degree of oxygenation permissible; it is without damaging effects upon the circulatory or respiratory systems. Clinically he has found the percentage of cyclopropane required to vary from 7 to 25, averaging 15 per cent cyclopropane to 85 per cent oxygen. He considers that the gas is a valuable anæsthetic, and hopes that further supplies will be soon available from German sources.—*Zentralbl. f. Chir.*, July 11, 1936, p. 1634. Abs. in *Brit. M. J.*

## Clinical and Laboratory Notes

### ENDOTRACHEAL ANÆSTHESIA SUPPLEMENTING AVERTIN IN OPERATIONS FOR CLEFT PALATE

By M. DIGBY LEIGH, M.D. AND  
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In operations for cleft palate the anæsthetic must be adequate, it must be safe, and its induction should not frighten the patient.

In an attempt to find a satisfactory form of anæsthesia, a series of cases has been operated upon, using avertin by rectum, and combining it with nitrous oxide administered through a large endotracheal rubber tube by the technique of Magill. This method is adequate for the purposes of the surgeon, because the operation field is not encumbered by the anæsthetist or the apparatus. From the anæsthetist's point of view it is efficient in that aspiration or swallowing of foreign materials is prevented, and, in addition, intimate control of the supply of oxygen and nitrous oxide to the lungs is provided. In emergency, artificial respiration is easily carried out by intermittent manual compression of the bag. In the second place, the method is a safe one. When all the various sources of danger in cleft-palate surgery are considered, it can be said that the anæsthetic itself creates the greatest hazard to life. Meticulous preparation before operation can counteract the perils of sepsis, anæmia, and dehydration. Efficient treatment after operation for shock and haemorrhage can be used, but the toxic effects of the drugs employed to produce anæsthesia always remain to be faced. There have been no deaths in the 32 cases covered in this report. The method has also been used in a large number of other operations upon the head and neck without misadventure. Thirdly, from the patient's point of view, this method of anæsthesia avoids the disagreeable features of ordinary induction

by inhalation. The avertin minimizes fear. A routine enema is always given before operation, and the child is not frightened when the rectal tube is again introduced some hours later for the instillation of the drug. Peacefully the patient slips into a sound sleep in its cot in the ward. After the operation it awakens in the same familiar surroundings. It has been saved the terrifying sounds and sights of the operating room and its environment. Avertin renders a special service in cleft lip and cleft palate, where a series of operations may be necessary, and where fear tends to be augmented with each successive trip to the operating room.

The procedure adopted is as follows. Prior to the operation the patient is examined in the ward by the anæsthetist, and the dose of avertin is calculated from the age and the weight. Infants are given 200 mg. of avertin per kilogram of body weight. The amount is reduced a little for each year, and at the age of twelve years, a dose of 100 mg. per kilogram of body weight is the standard. The weight of the child with respect to its age must also be taken into consideration. If the patient is found to be overweight for its age it is not advisable to give the full dose as calculated from age alone. Fat, or overdeveloped children should be given reduced doses. Conversely, children who are small for their age will require larger amounts of the avertin than would be indicated if age alone were taken as the guide. For example, a child twelve years of age, with the normal average weight of 36 kgm., would be given 100 mg. per kilogram; a small child of the same age, weighing only 28 kgm. should receive 150 mg. per kilogram.

The night before the operation the child is given its regular meal. About two hours later the lower bowel is carefully emptied by enema. The following morning, one-half an hour before operation, the determined dose of avertin is given in a 3 per cent solution. The largest soft rubber catheter that can be passed without dis-

comfort is introduced into the rectum. Using a funnel, the avertin is allowed to flow slowly into the bowel, and should the child struggle or cry the fluid can flow back into the funnel and not be lost. Ten minutes should be taken for the instillation. When the child is sound asleep a hypodermic injection of atropine sulphate is given to suppress secretions, and the patient is saved the pain of the needle puncture.

The patient is brought to the operating room. For palate operations a large thin-walled rubber catheter is passed through a nostril and made to enter the larynx, either by the "blind" method of Magill, or by the use of the laryngoscope and the Magill forceps. For lip operations it is passed through the mouth. If the first attempt to pass the tube through the larynx fails, open ether and carbon dioxide are administered to facilitate the intubation. As soon as the tube is in place it is wise to supply oxygen freely for a few seconds, and then to introduce nitrous oxide gradually. The pharynx is packed with a dry gauze sponge, to prevent blood from entering the stomach. The tube itself completely fills the glottis and protects the trachea. Partial re-breathing is carried out, using a bag about 12 inches from the face. Anæsthesia is maintained by supplying abundant oxygen with just enough nitrous oxide to keep the patient still. The use of avertin as a basal anæsthetic reduces the amount of nitrous oxide required, and, in consequence, increases the amount of oxygen that can be introduced into the lungs. Throughout the operation the patient remains in the supine position with the foot of the table slightly elevated. At the end of the operation the Magill tube is disconnected from the bag, and as it is withdrawn from the trachea, gentle suction is used to clear the air passages. To help restore body fluids and to combat post-operative acidosis, one-half to one pint of the fluid, as recommended by W. Bourne<sup>1</sup> in 1926, is instilled into the rectum. The patient is then returned to the ward. The arms are splinted to prevent interference

with the wound, and a nurse remains with the child until it is conscious. Voluntary movements usually begin within the first hour, and a small dose of morphia should be given if the patient becomes restless. Fluid nourishment, by feeder or pipette, is offered to the child as soon as there is any prospect of its being taken and retained. Solid foods are commenced as soon as possible.

#### SUMMARY

Since June, 1935, this method has been used in 32 cases, and the following information can be given:—

1. Age.—Youngest 7 months, oldest 14 years.

Ages	Number of patients
Under 1 year .....	4
Between 1 year and 2 years .....	3
Between 2 years and 3 years .....	6
Between 3 years and 4 years .....	7
Over 4 years .....	12
—	—
Total .....	32

2. Weight range—7 kg. to 56 kg.
3. Magill catheter passed through the nostril in 9 cases, through the mouth in 23 cases.
4. In three cases the avertin was partially expelled. Two of these patients were under 2 years of age. Expulsion can be stopped by squeezing the buttocks tightly together at the first sign of leakage.
5. Duration of operations, shortest 15 minutes, longest 90 minutes. Average time per operation 50 minutes.
6. Mortality: none.
7. Complications: one patient developed laryngitis and recovered in a week.

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EVIPAN SODIUM IN OBSTETRICS.—Dr. Van Boven strongly recommends evipan sodium anæsthesia for the short operations of obstetrics after an experience of about 150 cases comprising forceps delivery, internal version, suture of the perineum, Cæsarean section, etc. His dosage has never exceeded 10 c.cm., and for full anæsthesia is as a rule twice the amount needed to

produce relaxation of the jaw. The advantages claimed are the peaceful and pleasant introduction, ease and rapidity of administration, single-handed if necessary, wide margin of safety, rapid recovery, and absence of ill effects on mother or child. He has had no difficulties or accidents, and considers the only contraindications to be advanced pulmonary or hepatic disease—*Bruxelles Médical*, July 12, 1936, p. 1391. Abs. in *Brit. M. J.*

## Editorial

### ACETYLCHOLINE IN THE TREATMENT OF TOBACCO AMBLYOPIA

**T**OXIC amblyopia may be due to a considerable variety of agents, such as tobacco, alcohol, quinine, filix mas, carbon disulphide, nitro- and di-nitro-benzol, stramonium, cannabis indica, arsenic and lead. Of these causes the two first mentioned are much the most commonly met with.

The first references to tobacco amblyopia were made in Germany about the end of the eighteenth century; then in Scotland, in 1832, by Mackenzie in his "Diseases of the Eye". Since then much attention has been devoted to the subject but even yet it is not perfectly understood. We, however, realize that the ganglion cells of the retina and certain fibres of the optic nerve which pass from them are extremely sensitive to the action of various toxic substances. Some of these affect the peripheral cells and fibres and thus cause peripheral loss of vision, but the majority affect the central cells and fibres and cause central scotoma. Many years ago Uhthoff noticed the curious fact that while the toxins which cause central defects of vision are competent to produce peripheral neuritis also tobacco was an exception to the rule. The toxin in this case, therefore, exhibits a definite selectivity analogous to that of the diphtheria toxin for the palatal motor nerves and for the third nerve, and to that of lead for the musculo-spiral nerve. The end-organ of the auditory nerve in the cochlea is also susceptible, apparently, for Carroll and Ireland<sup>1</sup> have recorded that deafness frequently accompanies the amblyopia associated with the excessive use of alcohol and tobacco.

Writing in 1928, H. M. Traquair<sup>2</sup> states that among 108,142 ophthalmological patients in Edinburgh he found 1,088 cases of tobacco amblyopia (1 per cent). F. D. Carroll<sup>3</sup> in 1935, met with it in from 0.3 to

0.5 per cent of patients admitted to the clinic of the Massachusetts Eye and Ear Infirmary. These figures seem to support the statement recently made, that, despite the enormously increased consumption of tobacco in the past few years, tobacco amblyopia is not so often met with as formerly. This is probably due to the fact that tobacco is nowadays consumed very largely in the form of cigarettes. Tobacco amblyopia is much more common, as a matter of fact, among inveterate pipe and cigar smokers than in the cigarette addict. It has been found also in chewers and snuffers. In as much as the use of snuff appears to be gaining in popularity we should be on the look out for cases among the devotees. Tobacco amblyopia is much less frequent in women than in men, probably because the former indulge in the cigarette rather than the pipe or cigar. Carroll (*loc. cit.*) gives the figures as 2 females in a total of 55 patients (3.63 per cent), and Usher<sup>4</sup> found 2.5 of cases in females in a total of 1,100.

The amount of tobacco consumed in the Edinburgh cases (Traquair<sup>5</sup>) varied from  $\frac{1}{2}$  to 9 ounces weekly per patient, the average being about  $3\frac{1}{2}$  ounces. The smallest number of cigarettes found to produce the condition was 70 per week. Carroll and Ireland (*loc. cit.*), in 36 cases, found that the average amount of tobacco consumed was 8.9 ounces.

Some discussion has taken place as to whether so-called tobacco amblyopia is due to tobacco or to alcohol, for many excessive smokers also indulge freely in alcohol. Carroll (*loc. cit.*<sup>3</sup>) states that the average amount of pure alcohol consumed by his patients was 28.6 ounces per head weekly. He concludes that either tobacco or alcohol singly is competent to produce amblyopia. Traquair (*loc. cit.*<sup>5</sup>) thinks that, so far as Scotland is concerned, there is no relation-

1. CARROLL, F. D. and IRELAND, P. E.: Association of toxic deafness with toxic amblyopia, *Arch. of Otolaryngol.*, 1935, 21: 459.

2. TRAQUAIR, H. M.: Tobacco amblyopia, *The Lancet*, 1928, 2: 1173.

3. CARROLL, F. D.: Analysis of fifty-five cases of tobacco-alcohol amblyopia, *Arch. of Ophthalmol.*, 1935, 14: 421.

4. USHER, C. H.: An analysis of the consumption of tobacco and alcohol in cases of tobacco amblyopia, *Ann. Eugenics*, 1927, 2: 245.

5. TRAQUAIR, H. M.: Tobacco amblyopia, *Trans. Med. Chir. Soc. Edin.*, 1934, 35: 153.

ship between tobacco and alcoholic amblyopia, and gives what appear to be satisfactory reasons from clinical experiences for his opinion. No doubt, the two agents can act synergically on occasion. In any case, something more than a toxin seems to be necessary, probably a personal idiosyncrasy or some depressing external agency. Cases are known where those who have indulged excessively in tobacco for years with impunity have not developed amblyopia until attacked by some other illness or a digestive disturbance.

As regards treatment, naturally the first thing to do is to interdict the use of alcohol and tobacco. Drugs can be employed rationally only if we understand the pathogenesis of amblyopia, and, unfortunately, we are still somewhat ignorant of this point. So far as the early stage is concerned, inasmuch as patients do not seek advice until they themselves detect something wrong with their vision any pathological alterations in the eye are likely to be well advanced, and the initial manifestations will have been missed. We can draw conclusions only from ophthalmoscopic appearances, and then by inference. Even at this time the changes observed are slight, consisting in a congestive haze of the edges of the optic disc followed by undue pallor of the temporal side of the disc. In the one human case where the eye was examined microscopically the ganglion cells of the retina showed vacuolation and disintegration of the Nissl bodies with degeneration of the nerve fibres behind the lamina cribrosa. This degeneration was limited to the papillo-macular bundle. Possibly we are justified in concluding that the ophthalmoscopic picture is due to the occurrence of local atrophy of the retina plus an oedema which causes an anaemia from pressure. If so, we can justify the use of agents which can set up vaso-dilatation, as certain have advocated, such things as sodium nitrite and the presently popular acetylcholine.

Sir Stewart Duke-Elder,<sup>6</sup> who has investigated the subject experimentally, states that choline and acetylcholine act as powerful stimulants on the parasympathetic nerve

apparatus, producing contraction of the sphincter and ciliary muscle. They also dilate the small vessels, unless atropine has been exhibited previously, in which case a constrictor action is set up. In small doses choline lowers intra-ocular pressure; in large doses it causes a sudden and considerable rise in the pressure in the eye owing to the contraction of the extra-ocular muscles which is induced. Theoretically, on this basis, small doses of acetylcholine might be expected to do good in amblyopia by relieving pressure on the retinal cells and improving the circulation in the retinal blood vessels. The experiences of two or three observers may be cited in this connection. Bailliart and Rollin<sup>7</sup> report a case in which the left eye was affected; twenty injections of acetyl chloride were given with some relief of symptoms but no change in the field of vision. Marchesini<sup>8</sup> found, in six patients with retinal angospasm, that the administration of acetylcholine produced a fall of blood pressure much greater than normal, on the average amounting to 2.16/10 for right eyes and 1.5/10 for left eyes. Orr,<sup>9</sup> of Wolverhampton, has very recently reported on four cases of tobacco amblyopia which he treated with acetylcholine with gratifying success. All his patients were advised to stop smoking, but abstinence was not complete. He thinks that if his results can be confirmed by other ophthalmologists we shall have in acetylcholine the best agent for the treatment of tobacco amblyopia. On the other hand there are competent men who deny that vaso-dilator drugs are of any value in this condition. Only time will settle the matter. There is difficulty here in evaluating the effect of any drug, inasmuch as tobacco amblyopia, provided that abstinence is adhered to, is variable in its course and tends of itself to get well. If acetylcholine can speed up the process of recovery the case for it will have been made out.

A.G.N.

6. DUKE-ELDER, SIR S.: Recent Advances in Ophthalmology, P. Blakiston's Son & Co., Inc., Phila., 1934, p. 144.

7. BAILLIART, P. and ROLLIN, A.: Spasm of retinal arteries, *Bull. Soc. d'opht. de Paris*, 1935, Oct., 612.
8. MARCHESINI, E.: Retinal arterial pressure in relation to the general circulation and to certain ocular diseases, *Ann. di Ottol. e Clin. ocul.*, 1935, 63: 532 and 621.
9. ORR, H. C.: Acetylcholine in tobacco amblyopia, *Brit. M. J.*, 1935, 2: 69.

## POISONING BY MUSSELS

THE report that poisoning from eating mussels has occurred in Nova Scotia is of more than ordinary interest. Five cases have been met with, we are informed, of which two ended fatally. So far as we can learn, this is the first time within recent years, at least, that mussel poisoning has been met with in Canada. The occurrence is being investigated.

Between the years 1798 and 1928 there have been twenty-one outbreaks of this trouble in Europe and North America—10 in Great Britain, 7 on the Pacific coast of North America, 2 in Prussia, 1 in France, and 1 in Norway—embracing a total of 244 cases with 38 deaths.<sup>1</sup> In the California outbreak 102 persons were affected of whom 6 died. The species of mussel incriminated is the *Mytilus edulis* in Europe and the *Mytilus californianus* in California. Since then other cases have occurred in California, 55 in 1929, one in 1930, two in 1931, and 42 in 1932.<sup>2</sup>

Meyer, Sommer and Schoenholz<sup>1</sup> refer to a book entitled "Vancouver—A Voyage of Discovery to the North Pacific Ocean", London, 1798, in which an illness is referred to affecting several members of an English expedition to the north-west coast of America at a place now known as Vancouver. One death occurred. These authors say that the onset and course of the intoxication identify it with mussel poisoning as they saw it in 1927.

Poisoning from eating shell-fish may be divided into three categories: (1) cases due to allergic idiosyncrasy, which are attended by the relatively mild disturbances, urticaria and gastro-intestinal upset; (2) infective cases, due to contamination with various members of the *Eberthella* and *Salmonella* genera of bacilli—traceable to contamination with sewage; and (3) cases in which the nervous system is predominantly affected, manifested by paraesthesiae, paryses, and sometimes death from respiratory failure. The Nova Scotia cases fall into the last group.

Most textbooks mention mytilotoxin, a quaternary base, isolated by Brieger in 1888,<sup>3</sup> as the probable cause of the trouble, but subsequent observers have failed to identify the toxic substance found in the paralytic cases with Brieger's substance. The poison isolated from the cases in California is similar, chemically and pharmacologically, to the "fugu" poison of Japan, obtained from the liver and gonads of certain species of *Tetraodon*, which is used by the Japanese as a convenient and rapid method of committing suicide.<sup>4</sup> In nearly all cases the liver of the toxic shell-fish is enlarged, friable, and of dark colour, a fact that suggests the possibility of some disease condition, bacterial or metabolic. No bacteria, however, have been incriminated in the "paralytic" cases, though, it must be said, the possibility of a virus being the cause has not been excluded. Inasmuch as the toxic mussels in the California outbreaks were always full of spawn Meyer, Sommer, and Schoenholz (*loc. cit.*) thought that the toxin was a "sex poison". Suggestive analogies are found in the fact that the roe of some fish of the sturgeon family is poisonous during the spawning period. Prinzmetal, Sommer and Leake,<sup>5</sup> on the basis of experimental evidence, think it unlikely that the poison is histamine. Mussel poison is many times more toxic for mice than histamine on intraperitoneal injection, and differs from histamine also in the fact that it has no noticeable action on smooth muscle. In general it resembles curare and is probably a quaternary (or possibly tertiary) amine. The toxic material from the poisonous mussel is slowly absorbed from the gastro-intestinal tract and is rapidly excreted through the kidneys. Its main action seems to be to depress respiration. The cardio-inhibitory and vasomotor centres are also depressed, as is the conductive system of the myocardium.

1. MEYER, K. F., SOMMER, H. and SCHOENHOLZ, P.: Mussel poisoning, *J. Prevent. Med.*, 1928, **2**: 365.
2. MULLER, H.: Mussels and clams: a seasonal quarantine: bicarbonate of soda a factor in the prevention of mussel poisoning, *California and West. Med.*, 1932, **37**: 263 and 327.

3. BRIEGER, L.: Zur Kenntnis des Tetanin und des Mytilotoxin, *Arch. f. path. Anat. u. Physiol. u. f. klin. Med.*, 1888, **102**: 549.

4. PHISALIX, M.: *Animaux Venimeux et Venins &c.*, Masson, Paris, 1922.

5. PRINZMETAL, M., SOMMER, H. and LEAKE, C. D.: The pharmacological action of mussel poison, *J. of Pharmacol. and Exper. Therap.*, 1932, **46**: 63.

6. MULLER, H., *loc. cit.*

Soon after the ingestion of poisonous mussels, and the more quickly if the stomach is previously empty or if no other food is taken, the patient notices numbness of the mucous membrane of the mouth and numbness and pricking of the fingers and toes. Then, incoordination of the movements of the limbs, ataxic gait, and incoordination of speech are noted. The early manifestations have a striking resemblance to acute alcoholism. The mind is clear, but the patient may feel exhilarated and may not realize the seriousness of his condition. Nausea, vomiting and diarrhoea are occasional phenomena. A gripping sensation in the throat and respiratory distress have been observed. In fatal cases pareses of the musculature of the neck and limbs, with dyspnœa, and, finally, respiratory paralysis may occur. Death has occurred in as short a time as three hours. The average temperature is slightly subnormal; the pulse is increased in rate, from 80 to 100.

The treatment consists in washing out the stomach with a solution of bicarbonate of soda and the exhibition of saline cathartics, such as Epsom salts, and powerful diuretics. If the depression of the respiratory centre is marked carbogen and coramine are indi-

cated; artificial respiration may be called for. Digitalis and alcohol should not be used.

The greatest number of cases of mussel poisoning occur in summer, in some years as early as June and as late as September. Consequently, the California Board of Health has instituted a quarantine on mussels during the summer months every year since 1927, and a few years later this was extended to cover clams, which also have been found poisonous at times. The usual methods employed in cooking mussels and clams do not lessen the danger of poisoning. The water in which the shell-fish are boiled or which remains in the shells should be thrown away, as it contains a large proportion of the poison. The addition of soda bicarbonate, a tablespoonful ( $\frac{1}{4}$  oz.) to each quart of water in which the mussels are cooked, is advisable since boiling continued for 20 to 30 minutes destroys 85 per cent of the poison, though it does not altogether obviate the danger. In the case of both mussels and clams the poisonous substance seems to be confined almost entirely to the intestines, so that these organs should be removed before the shell-fish are cooked. This is an easier procedure in the case of clams inasmuch as in them the intestines are relatively large and easily detected.

## Editorial Comments

### The British National Human Heredity Committee

In England, a National Human Heredity Committee has been formed, composed of R. Ruggles Gates, Sir Humphry Rolleston, Grafton Elliot-Smith, R. A. Fisher, Sir Arthur Keith, and Sir F. Gowland Hopkins. They have sent a letter to the Editor of the *London Times* which reads as follows (quoted from *Science*, June 5, 1936).

"Problems of national health have reached a point where the hereditary element can no longer be neglected. The leaders of the medical profession are no longer satisfied with the alleviation of disease but are acutely conscious of the need for fuller knowledge of heredity in connection with its prevention. This applies not only to the transmission of defects. It is recognized that methods of cure must vary with the type of constitution of the patient, and in this connection information concerning heredity is of great importance. In education, in training, and

in choice of career the ascertainment of innate endowment not only prevents waste and failure but would contribute largely to the attainment of success.

"The instructed public already recognize the importance of heredity for the future of the race, and the Brock report in 1933-34 emphasized the need for greater knowledge in regard to the inheritance of mental and physical defects. But there is as yet no centre to which the public can turn for full information.

"The Imperial Bureaus of Plant Genetics (in Cambridge and Aberystwyth) and of Animal Genetics (in Edinburgh) have achieved much by setting up simple machinery for collecting information based on the results of research and making these available for the practical breeder. The Bureau of Human Heredity which has recently been set up at 115, Gower Street, W.C.1, follows these models, and small contributions have already been made for its upkeep.

"In these days of international mistrust and animosity it is refreshing to find a field in which

representatives of nearly every civilized nation are engaged in cooperative work. The scheme for an international clearing-house of facts concerning human heredity has been evolved by a small international committee, which has delegated to its British members the task of setting up a bureau in London for the collection and distribution of all authentic information on human genetics. The British Council is asking for £10,000 to carry on this work for five years.

"It is strange to think that students of fruit-flies or mice have at their command the latest information, while those similarly concerned with man can look nowhere for a complete survey of the knowledge they require. The urgency of this need leads us to commend the Bureau of Human Heredity to public-spirited donors. They will find no institution the endowment of which will give a more liberal return for all time."

For some years, we have been urging upon the medical profession, especially those connected with the teaching of medicine, that a course in Medical Genetics be included in the medical curriculum, which will enable the physician of tomorrow to be more conversant with the subject of heredity in man than he is at present. As Lord Horder has said, there would be time for such a course if other subjects, less important than human heredity, were left out of the curriculum or curtailed in time. It is to be hoped that Canadian medical schools will sponsor such a course in medical genetics (this subject is already being taught in several of the leading American schools), and that Canadians in general will sponsor such an institute for the study of human inheritance as has been founded in many of the European countries and is now being founded in England. The distinguished names on the committee in Great Britain may be taken as an index of the importance of the plan they urge. Why should not the Canadian medical profession get behind the same movement in Canada?

MADGE THURLOW MACKLIN

#### Medical Science Exhibits

We have become so accustomed to the medical exhibits at annual conventions that we take them for granted. And yet, it is doubtful whether medical men in general realize what work lies behind them or how greatly the technique of their presentation has improved. Those

Generally speaking we might say that the diseased employ a language which corresponds to thinking, to concepts that are at a lower level, or at least of a different order of abstraction. Just as one cannot measure apples by a foot-rule nor describe books in

who attended the Conjoined Meeting at Atlantic City last year had full opportunity of seeing these things for themselves, and we understand that the exhibits at the Kansas City meeting of the American Medical Association this year fully sustained the standard set.

We are reminded now of the medical exhibits at the Century of Progress Exhibitions in Chicago, in 1933 and 1934, by a booklet\* in which they are preserved in pictorial form. One cannot look through it without a freshened sense of the importance of such exhibits. These at the Chicago Exhibitions were unusual in being the first attempt of the kind in connection with an international exhibition in America, but the principles underlying their value were the same.

In getting out this most attractive booklet the aim has been to prolong the influence of these exhibits and also to help towards the foundation of permanent museums of health. The value of such can hardly be overestimated in instructing public opinion in matters of general health. They serve also to show the public just what immense and varied labour lies behind the training of the qualified practitioner, nurse, dentist and pharmacist, serving to sharpen the contrast between them and the untrained quack. We can only add that the pictures of which this book is composed entirely and most attractively perform their function in describing the variety of the exhibits, incidentally causing one to marvel at the labour they must have entailed. H.E.M.

#### Income Tax Allowance for Automobiles

We are in receipt of a letter from Mr. C. F. Elliott, Commissioner of Income Tax, Ottawa, addressed to the General Secretary, which reads as follows.

"With regard to Clause 2 (i) of the Memorandum regarding Returns of Members of Medical Profession, issued under date of 28th February, 1933, wherein it is stated that as an alternative to (h) and (i) there may be allowed a charge of 10 cents per mile for automobiles used in the performance of professional duties, it may be said that as a result of experience since that memorandum was issued it is felt that the 10 cent per mile is a too liberal allowance, and while it is not proposed to reduce this allowance retroactively, yet the Department has come to the conclusion that for 1936 and subsequently this allowance shall be reduced to 8 cents per mile."

\* Medical Science Exhibits. Eben J. Carey, Sc.D., M.D. 204 pages, illustrated. Price \$2.00. Copies may be obtained from Patrick J. Byrne, 624 S. Michigan Ave., Chicago, 1936.

terms of Turkish rugs so the language of disease is not susceptible of a literal, word-for-word translation into the language of the well. A translation of what the sick person is trying to convey in what he says is quite the same sort of process as the translation of a primitive language.—White, *The Meaning of Disease*, p. 180.

## Special Article

### THE RELATION BETWEEN PSYCHOLOGY AND MEDICINE\*

BY S. R. LAYCOCK,

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Saskatoon*

Because there are so many misconceptions of the nature of psychology, and because psychology has undergone in the last few decades a change amounting to a revolution, I feel that I must begin my address by a brief statement of what psychology really is. First of all, it is not, as it was in the university days of some of the members of this audience, a branch of philosophy. As you know, all branches of knowledge were once a branch of philosophy. In the days of the Greeks, physics, chemistry, astronomy and geology were all parts of philosophy. Leucippus and Democritus, for example, expounded the atomic theory of matter as philosophers. Anaximenes, a philosopher, thought the visible dome of the sky was half a complete sphere with the earth at the centre. Empedocles, a philosopher—not a chemist—thought earth, air, fire, and water were the basic elements out of which all other substances came. One by one the sciences of physics, chemistry, astronomy, biology, left the parental roof of philosophy and set up in business for themselves. Psychology was one of the younger members of the family, one of the last to leave. In other words, in the last few decades psychology has become a science.

The difference between science and philosophy is this. In philosophy the results are obtained by speculation and introspection, in science, by controlled experiment; in philosophy deductive reasoning is very common, while in science there is the inductive approach. The scientific method involves (1) accurate observation of a large number of facts, (2) classification of those facts, (3) the formulation of a hypothesis to explain the facts, (4) verification of the hypothesis, (5) the formulation of general laws. Psychology is rigorously trying to follow this method. A science is not characterized by the nature of its subject matter but by the method of its attack.

Psychology has had a harder job in making progress than the older sciences because it has had to combat theories about human nature and conduct and about the human mind which are very thoroughly established and which are the results of theological and philosophical

speculation. For example, in the field of the law jurists had to have theories about human nature before scientific psychology could supply them, and, as a result the law is established on deductive and theological conceptions, and the time has now come when all legal conceptions have to be worked over in terms of modern psychology—such doctrines as responsibility, free will, motivation, etc.

Next I want to say that psychology is not a science of the soul or of the mind, since no one knows the nature of these, nor is it the science of consciousness, as some of you learned in your university days, since there is a whole psychology of the unconscious. Rather modern psychology regards itself as the science of *behaviour*, and by behaviour it means muscular, glandular and cortical reactions. It accepts as its fundamental hypothesis the foundation of *all* science, namely, that of cause and effect. The natural scientist assumes in the material universe that cause and effect operate, and all advance has been made on that basis. Similarly, scientific psychology, leaving aside mysterious problems of free-will, intuitions and "hunches", objectively studies behaviour on the assumption that *all* behaviour consists of reactions to stimuli. In primitive times behaviour was considered as the result of one of three agencies—(1) human agencies by magic, (2) supernatural agencies, (3) natural causes. The man on the street still thinks of human behaviour in these three categories, but modern scientific psychologists go only on the last—natural causes.

Our approach to behaviour and conduct disorders is now the same as yours, *i.e.*, the diagnostic point of view. When you, as physicians, go to see a patient and you find he has a temperature of 102° you do not just say "naughty, naughty", you proceed to diagnose the underlying causes. Similarly, the clinical psychologist dealing with a behaviour problem like stealing regards it as merely a *symptom* of social maladjustment and proceeds to look for underlying causes. Courts and parents and even teachers often treat *symptoms* instead of underlying conditions. For example, you as physicians may have ten patients all with a temperature of 102°. How ridiculous it would be if you stopped at the taking of the temperature and gave all the same medicine. But that is what has been done with behaviour. Stealing isn't just stealing—it may be due to as wide a variety of causes as a temperature of 102°. Child Guidance Clinic annals reveal that stealing may have its roots in the child being undernourished and not having enough food, in sex-behaviour and conflicts, in subtle motives of revenge against parents, in attention-getting mechanisms, and in compensations for feelings

\*An address delivered before the Prince Albert and District Medical Association on December 10th, 1935.

of inferiority occasioned in dull children by our present uniform curriculum, organization and teaching methods in schools. If I had time I would show you how truancy is just a symptom of school maladjustment, due to a large variety of causes, and how laziness, inattention, and lack of concentration are just blanket terms for lack of interest and where underlying causes must be sought.

I wish, too, that I had time to show you in some detail the things we use in diagnosis. You, as physicians, use a wide range of examinations in diagnosis—increasingly objective—blood counts, urinalysis, basal metabolism, x-rays, etc. I would have liked to have told you how I use the facts of the school history, the results of the medical examination, intelligence tests, achievement tests, reports and ratings by teachers, reports and ratings by parents, developmental history, family history, and an interview with the child.

May I point out we are moving in the same direction as medicine, towards increasingly objective and scientific methods in diagnosis.

And now let me turn to the other part of my address, the relation between psychology and medicine. I am not going to enter into the ancient controversy—the mind-body controversy, though it is obviously very important what you think about it. Perhaps it is sufficient to say that the Christian Scientist who denies the existence of matter and affirms the universality of mind, and who replaces all medical treatment of disease with a system of faith cure or mental treatment, is not much worse than a thoroughly materialistic *materia medica* which limits the healing art to the drug or surgical treatment of the malfunctioning organ, and which undervalues or completely neglects the treatment of the patient as a whole, as a functional unit. Fortunately, this crass materialistic treatment, followed, I hope, by a limited number of the disciples of medicine, is now declining.

Modern psychology conceives of the human organism as a highly complex ensemble of mental and physical traits and functions that are inextricably intertwined and interdependent. It believes that these factors exert a reciprocal influence upon one another and are mutually affected by numerous environmental and hereditary influences which conduce towards mental soundness and unsoundness. The human organism is a psychophysical unity. The physical and mental are merely two aspects of the same unitary organism, just as the obverse and reverse are merely two sides of the same shield, the one as indispensable as the other. If, then, the assumption is correct that the body and mind are mutually interdependent and interacting aspects of a single organism it logically follows that any program for the attainment of health that neglects either the mental or physical factors is incomplete and unsatisfactory.

I do not need to remind you as physicians of the influence of the so-called physical aspect on the so-called mental aspect of the organism. Bodily diseases, injuries and defects sometimes produce sudden and profound mental disturbances, and therefore seriously affect behaviour. As examples of this I may cite the following: delirium as an effect of fever; a blow on the head or the bursting of a cerebral blood vessel may produce sudden stupor or unconsciousness; excessive fatigue may produce inattention, muscular incoordination, memory lapses, temper tantrums; jaundice does not conduce to generosity or philanthropy; heart sensations may induce anxiety and apprehension; disturbances in the endocrines always have mental concomitants; for, example, excessive thyroid secretion in exophthalmic goitre tends to induce nervous and mental instability, sleeplessness, emotional instability.

Another line of evidence in regard to the effects of the physical upon the mental concerns the influence of foods and drugs upon mentation. Certain foods, even such as milk, eggs, or mushrooms, may in certain cases produce epileptic convulsions. Certain foods have been found to inhibit sex activity in rats. The effects of alcohol, inducing loss of motor control, thick speech, mental confusion, forgetfulness, excitement, depression, etc., are well known. I do not need to multiply instances. You know more than I do in this field.

But what about the influence of the mental upon the physical? Here I think, too, the evidence is indisputable, not only for the widespread somatic reverberations of emotional experiences but also so far as it concerns the mere emotionless thinking or attentive states upon the circulation of the blood or upon motor innervation. That mere thought or ideas can affect the circulation of the blood through the excitation of the nervous system can be shown by the well known balance board experiment. In this experiment the subject, while lying quietly upon a perfectly balanced platform, is asked to read an unemotional passage of prose or solve a mathematical problem. After a brief interval the experimenter will observe that the end of the board on which the head rests gradually begins to descend. Obviously, thought has affected the circulation; it has caused the blood to flow to the head, in consequence of which the head grows heavier and the board begins to tilt.

Similarly, if attention is concentrated upon an active muscle the flow of blood can be increased to that muscle. The effect of attention upon the circulation can be most convincingly shown in states of hypnosis in which the subject becomes highly susceptible to suggestion. In some cases the mere suggestion by the hypnotist that the subject has a scar or burn on the arm may produce a localized area of hyperæmia on the skin. This is the obvious explanation of many hysterical symptoms. However, the most

striking illustrations of the influence of the mental upon the physical are not derived from a consideration of processes of calm logical thinking or of perceiving and attending. It is when mental processes are closely connected with instinctive functions and glandular activities that the effect of mental states upon physical conditions become more clearly apparent. In a general way, any mental activities that stimulate the endocrine glands will exert a subtle influence that may pervade the whole organism and sometimes may produce the most profound organic disturbances. The extreme sensitivity of some of the glandular functions to mere ideas or perceptions is well recognized. In some persons, for example, the sex centres in the brain and the cord are so responsive that mere images and thoughts can serve as adequate erogenous stimuli. Also, the mere thought or perception of appetizing or unappetizing foods or of savoury or unsavoury odours is sufficient to stimulate the salivary or gastric nervous centres in many persons.

Wallin quotes a well known experiment upon a dog in which the gastric secretion was diverted into a container instead of the stomach. An undisturbed, pleasurable five-minute feeding resulted in the secretion of 66.7 c.c. of gastric juice in from fifteen to thirty minutes. On a later occasion, when the dog became excited by being shown a cat just before the feeding, no secretion occurred during the five-minute feeding period, and the secretion amounted to only 9 c.c. in the following twenty minutes. Emotional excitement inhibits the flow of gastric juice.

Emotional experiences are the chief cause of nervous dyspepsia or acute indigestion rather than the food ingested. An instance, cited by Wallin, is that of a woman brought to the hospital because of an attack of acute indigestion. It was found the following morning that the evening meal had remained in the stomach all night. Further investigation disclosed that she had been upset in the evening by a quarrel with her husband who had come home drunk.

The profound organic commotion that can be produced by intense emotional experiences can be illustrated by fear. Not only is fear evidenced by trembling, shrinking, raising the eyebrows, irregular breathing, and by movements of escape or combat, but also by inner conditions such as dryness of the mouth due to inhibiting action upon the salivary glands, inhibition of the flow of gastric juice, and acceleration of heart action with consequent rise in blood pressure.

Cannon has found in experiments that the strong emotions—fear, rage, excitement, anxiety, worry—cause the adrenal glands to discharge excessive amounts of adrenalin. This seems to shut off the activities of digestion and stimulates the heart and lungs to strong action. Further, it makes the liver secrete its store of blood sugar

required by the muscles. In other words, the strong emotions constitute a calling out of the troops. In primitive days when attacked by an enemy the animal had to mobilize all its reserves for either fight or flight. And it could afford to have its digestion switched off temporarily, since, obviously, if one was to be eaten by a beast of prey it wouldn't matter whether one's dinner digested or not. In contradistinction to the strong emotions which deplete the body reserves, the mild emotions of mirth, joy, goodfellowship, stimulate the digestive activities and to some extent allow the troops to loaf in barracks. In other words, the strong emotions use up reserves and the mild emotions build them up. This has tremendous implications for physicians in two ways. (1) The effects of emotional upheavals of fear, anger, rage, grief, worry, and anxiety may give rise to or at least aggravate stomach trouble, indigestion, metabolic disturbances, diabetes or glycosuria (mentally disordered persons subject to fears often suffer from diabetes), overaction of the thyroid and adrenal glands, loss of vitality, jaundice, heart disorders, degeneration of the liver, insomnia and dysentery (a defeated army suffering from dysentery is more likely to be suffering from mental collapse than from intestinal infection). Symptoms which simulate those produced by organic disturbances are everywhere to be found.

The exhausting and disturbing effects of emotional upsets upon the nervous, glandular, digestive and circulatory systems may lead to nervous exhaustion or hyperexcitability as well as to nervous maladies. Nervousness in general is due more frequently to emotional stresses and adjustment difficulties than to physical disease or injury, although physical derangements aggravate the condition. Nervousness is not really a disease of the nerves. It is a disorder of function rather than a defect of structure. It is more of an emotional than a physical disorder. Ninety per cent of the cases of shell shock in the World War were due not to any physical injury received in battle, but to disturbed emotions and to emotional collapse from fear, anxiety, dread, and the desire to escape from the battle front. J. W. Barton has estimated that over fifty per cent of all patients consulting physicians or seeking hospital treatment have no real organic trouble. E. A. Strecker believes that fully fifty per cent of the problems of the acute stage of illness and seventy-five per cent of the difficulties of convalescence have their primary source in the patient's mind rather than in his body. Maurice Craig says that from fifty to seventy-five per cent of the patient's illness may be due to his attitude towards his disorder. It is notorious that the patient's attitude to his illness is often harder to treat than the sickness itself.

I like to think of the word disease in its root meaning, dis-ease. Now dis-ease may be either physical or mental. It will be obvious

from the above that no physician can hope to treat his patients adequately unless he is first of all willing to recognize that emotional upsets and conflicts, strains, shocks, worries and anxieties may be at least definite contributory causes to the disorder he treats. His diagnosis is incomplete without a psychological diagnosis, and his treatment is incomplete without psychological treatment.

Most physicians pick up quite a bit of practical psychology from practice, but it is also true that most physicians are quite innocent of the findings of modern psychology or of recent developments in psychopathology and psychotherapy. It is not enough to use this unconsciously. The medicine man of primitive tribes and the Christian Science practitioner use psychology unconsciously. Speaking as a layman, may I humbly suggest that training medical students in psychiatry, which usually means the psychotic condition of advanced mental disease, is not enough. What a medical student needs is a grounding in the psychology of the so-called normal people—the people who come to his office from day to day. Psychology as an applied science now exists and it can be applied to medical practice.

(2) A second implication of any discussion of the effects of emotional stress on physical condition lies in the fact that since fear, for example, calls out the body reserves and the body-destroying processes, and since the mild emotions of mirth, joy, and goodfellowship call out the body-building processes, then it is the physician's duty to get nature working with him and not against him. Confidence in the physician is therefore of great value. When patients come to you and talk to you they often go away feeling much better because they have talked to you, even when you have given them no medicine or treatment, because you have removed their fear and let nature have a chance. You visit your sick patients regularly not only because it is necessary to see how they are getting along but to remove their fear and anxiety and give nature a chance to work. Apart entirely from the legitimate uses of medicine, x-rays, etc., there may be definitely a beneficial effect because they remove fear and lurking unknown terrors. Doubtless, a host of patent medicines and quack remedies flourish because they have helped people through the removal of fear and letting nature have a decent chance. May I respectfully suggest that until the science of medicine is able to take up into itself psychotherapy, and to do it wisely, quacks of all sorts will continue to flourish.

All of this will have to be handled with skill and understanding. There is always the danger in connection with even such worthy causes as the cancer campaign that, in trying to educate people, you merely succeed in implanting fears, with all sorts of disastrous results.

Sometimes, too, physicians, instead of inspiring confidence in themselves, succeed merely

in making the patient believe he is terribly ill, with consequent fears. It is a bit of a dangerous game to play a corresponding role to some professional evangelists who work up guilt feelings in order that they may prescribe their own pet remedy. In fact, the treatment given a patient sometimes depends on the personality and personal maladjustments of the physician as well as on the condition of the patient. Already it is advocated that all teachers have a psychiatric examination before being licensed. Some day this will also apply to nurses and physicians.

I am far from suggesting that fear and anxiety are the only mental elements in producing disease. Mental conflicts of all sorts are fruitful sources of illness. Some are conflicts over sex; some are conflicts over the attitudes towards the self; and many illnesses are unconsciously wished for illnesses which offer a way out. An example of this, quoted by Wallin, is that of a badly pampered young man, of somewhat unstable type, who began his career as an accountant. Before many weeks he was brought home complaining of severe pains in the eyes and in the right arm, which seemed partly paralyzed. Feeling better after a few days' rest, he returned to work, only to find the attacks recurring. The significant thing about these symptoms is that they made his work at the office impossible. Actually, the young man found the tedious task at the desk, day in and day out, extremely boring, and the work deprived him of the freedom and comforts which home life had previously given. At the same time, he was naturally averse to quitting outright. That would offend his self-respect and bring the scorn of his friends as well. Perhaps one afternoon the fatigue of eye and hand did become severe, providing an excuse for release from labour for the day. The next day the same symptoms occurred in more severe form, and half frightened, and yet half gratified, he was taken home. Not only did he thus escape the unpleasant work but the criticism of himself and others as well. In fact, he reaps more sympathy and care than ever. To refer again to the neuroses of the war. All sorts of *physical* symptoms, paralysis of the arm, temporary blindness, vomiting, etc., provided an unconscious defense mechanism. I am not maligning soldiers, for I am a returned man myself.

Faith cures of all sorts, which since the days of the medicine man of primitive tribes and of heathen rites and the oracle at Delphi down to modern Christian healing, are not mysterious cures of a supernatural order; they are a species of psychological healing in which either (1) the conflict is resolved, or (2) the patient gets more satisfaction out of being well than out of being sick, or some similar psychological process. These forms of healing often embarrass medical men. They should not. The problem is not solved by saying it is just "mental". The medical profession must do the same thing, only scientifically, and, if scientifically, in the long run better.

We need psychotherapists—medical men who really know a lot of normal and abnormal psychology—not merely medical men trained in the end-product of mental disease. And since the individual functions as a psychophysical unity no physician can treat just *physical disease*, he must treat *persons*. Whether you realize it or not, you *must* use the psychological element in your work. My plea is that the medical profession use it scientifically and consciously instead of empirically and unconsciously. Many hospitals now use the services of a social worker as part of their therapeutic service. May I suggest that the time will come when every physician with a large practice will have a trained social worker to assist him.

May I suggest also another point of view. Just as it would be difficult for you to divide the population into two classes, the sick and the well, but rather into a whole series of less and more well, so a study of individuals on the mental side presents a continuous gradation all the way from so-called normal people to the violent patient in the mental hospital. The differences between the insane and us are only those of degree not of kind. Differences are quantitative, not qualitative. Everything we have in a mental hospital we have in milder degree in life. Grandiose delusions are but an extreme form of the "limelightness" of some school children, and everyone of you knows persons, accepted as good citizens, who think of themselves more highly than the facts warrant. Paranoid delusions have their counterpart in life in many individuals who are very suspicious and who think that everyone is "down" on them. Self-pity, found abundantly in school children and in a large percentage of adults, is merely a mild form of paranoid delusion. The child with temper tantrums and the adult who goes "clean off his head" with rage are milder forms of a manic phase found in mental hospitals. So psychologists and mental hygienists think of self-pity, temper tantrums, sullenness, sulkiness, shyness, limelightness, feelings of inferiority and superiority, resentfulness, pouting, as mild disorders, all more or less mental. So the problem of the prevention of mental disorders goes down into early childhood into the school and home, and it isn't only their mental health—it's their *health*. No child can be said to be *healthy* when it suffers from such emotional maladjustments as described above.

In conclusion, may I make a plea for the treatment of behaviour, personality or conduct disorders on an objective basis. To tell persons with neuroses that they are ridiculous or silly or blameworthy doesn't solve the problem. Rather these people need diagnosis, understanding and *treatment*. To tell a person with a pain that it is just imaginary and he is to forget doesn't solve the problem. It only sends him off to another doctor or, worse still, to the quacks.

One must, however, be equally warned against the opposite extreme, *i.e.*, admitting that the patient has a pain and pretending to know all about it, ascribing it to an organic source and operating, leaving the patient no better. If there is no organic basis for the pain there may be a psychological one, and telling the patient to forget it does not remove it in this case any more than when there is a physical basis. The people with neuroses are not to be made to feel inferior and culpable. They need and deserve treatment just as your other patients need and deserve treatment.

To assume that *all* forms of behaviour are amenable to the law of cause and effect is the approach of a scientist. Medical men must treat individuals, and the day must come when their understanding and therapy are as scientific in the so-called mental realm as in the so-called physical realm.

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#### SOME PERSONAL IMPRESSIONS OF THE MEETING OF THE BRITISH MEDICAL ASSOCIATION HELD IN OXFORD IN JULY, 1936

BY ROBERT DAWSON RUDOLF,  
Toronto

The 104th Meeting of the British Medical Association was held in the classical surroundings of Oxford this year and was as usual well attended and a great success. The first few days were taken up with the work of the Council, and most parts of the Empire were here represented, but Canada had no voice. It seems to be a pity that the numerous members of the Association who live in Canada should have no say in such an important conference, but such is at present the case. The delegates from the Canadian Medical Association (Drs. Birkett, A. H. Gordon, and the writer) were of course welcomed and duly presented to the President at the Annual Meeting, but they had no official position as representatives of the members of the Association in Canada, and therefore no *entrée* to the Council meetings where all the activities of the Association are formulated.

The Meeting proper commenced on Tuesday, July 26th, with the masterly Address by the President, SIR FARQUHAR BUZZARD, entitled "And the future", which appears in full in the *British Medical Journal* of July 25th.

The numerous Sections met in the University Museum and were well attended. I could be present only at those of Medicine, and Pharma-

cology and Therapeutics, and hence can only speak of the work done there.

*The Section of Medicine.*—The whole of the first morning was devoted to a consideration of "The treatment of chronic rheumatism, articular and non-articular." DR. TIDY, of London, opened the discussion by saying that he regarded rheumatoid arthritis, osteo-arthritis and fibrosis as all coming under the term "chronic rheumatism". A septic focus should be looked for, and only when such was definitely present was vaccine therapy justified. The only drug that had any specific action here was gold, but its use required great care. Schemes of dieting had their chief action in alteration of weight. He did not think that thyroid extract had any specific effect. In the acute stage absolute rest was necessary, and a single daily movement of each affected joint should be instituted, to lessen deformities and adhesions. During the rest of the time splints were required. Heat in various forms was of great value. He was sceptical of the special effects claimed for the various spas except as regards the external use of waters. All physical and balneo-therapy should be directed by a medical practitioner.

DR. ABERCROMBIE, of Sheffield, thought that the psychological element was important. The confidence of the patient should be reinforced.

DR. BUCKLEY, of Buxton, regarded the prolonged use of moderate warmth as of more use than short spells of greater intensity. He approved of the dictum of Openshaw that flannel bandages were of greater value than more complicated applications. Massage often inflicted new trauma on the tissues already inflamed. Although some absorption of certain drugs took place through the skin the stimulation of the skin was the chief factor in local applications.

DR. GIRDLESTONE, of Oxford, would separate the polyarticular fusiform type of rheumatism from the periarticular form associated with round-celled infiltration. The former required very slow passive movement, while the latter needed manipulation in its later stage to break down adhesions.

DR. KERR PRINGLE, of Harrogate, thought that gout was often missed nowadays, and believed that many of our cases were of metabolic origin.

DR. POTTER, of Buxton, distinguished between active and passive congestion of the joints. The former had increase of pain during movement, while the latter were worse during rest. Counter-irritation was of value in the active congestive forms. Several others contributed to the discussion but brought out nothing new.

DR. TIDY, in reply, said that he was "still unrepentant on the subject of spa treatment".

The second morning was taken up with the subject of "Flatulence and epigastric discomfort". PROFESSOR RYLE, of Cambridge, opened the discussion by calling attention to epigastric discomfort rather than pain. The history was

of great importance, and we should listen to the patient's own description of his sensations with great care, for from it we could often come near to a complete diagnosis of the underlying cause. Gastric flatulence might be odourless or foul; the former usually being due to aerophagy and the latter to some organic trouble.

DR. J. M. H. CAMPBELL, of Oxford, considered cases of acute indigestion occurring at night and with no history of previous gastric trouble as often being cases of coronary thrombosis. Many patients with this serious trouble were treated for indigestion.

DR. THOMAS HUNT pointed out how often intestinal (and colonic) conditions caused epigastric discomfort. The sense of fulness often felt by people after a very small meal was due to a failure of the normal gastric relaxation.

DR. A. F. HURST discussed the mechanism of aerophagy, and considered that many cases of epigastric discomfort were due to gaseous distension of the splenic flexure of the colon. This might be relieved by reducing the starch content of the diet. An abnormal valvular mechanism at the cardia may cause the condition of "air-lock" in the stomach.

DR. JOHN PARKINSON was often impressed by the absence of the complaint of "wind" where this might be expected from the distension of the stomach seen with the x-ray. Pain in the chest on exertion was nearly always of anginal origin.

COLONEL STOTT, of Lucknow, said that epigastric discomfort was common among the natives in India and was due to excessive carbohydrate diet. Several others took part in the discussion, and PROFESSOR RYLE, in winding it up, said that he considered aerophagy as a conditioned reflex developed in an attempt to dislodge wind that the patient thought was there.

On the last morning the Sections of Medicine and Surgery combined in a discussion of "The surgery of pulmonary tuberculosis". DR. JOHNS GRAVESEN, Medical Superintendent of the Vejlefjord Sanatorium, Denmark, first read a most comprehensive paper, which appears in the *British Medical Journal* of August 8, 1936. He began by saying that all attempts at directly attacking the disease surgically, for example, by drainage of cavities or lung sections, have long ago proved fruitless. The only method that need be considered was artificial pneumothorax and only when this was impossible on account of adhesions were the removal of these adhesions or other more radical operations necessary. All these proceedings were with the object of allowing relaxation rather than compression of the affected portion of the lung. Such relaxation acts by permitting the natural tendency of the cavities to contract. So long as the tuberculous process is active any major surgical intervention is contraindicated. The condition favourable for operation is where the temperature is more

or less normal and the weight stationary or increasing. Blood sedimentation gives some information about the development of resistance, and serial examinations of the blood picture, the leucocytes being counted by the Arneth or Schilling methods, even more. The theory of relaxing the tension and so allowing the cavity to contract has greatly modified the technique of procedure. Our object should be not to completely collapse the lung, much less to compress it, but to relieve local tension in the diseased area, while allowing the healthy portions of the lung to function. A pneumothorax, when large, tends to compress the healthy parts, which is not what is required. What we want is "selective relaxation". This is usually best done by division of adhesions, but where this fails more radical attacks on the chest wall may be required. In rare cases apicysis is of value. The speaker strongly condemned evulsion of the phrenic nerve which paralyses the diaphragm and thus reduces the function of the lower part of the lung, which is usually not the site of the cavity.

DR. F. G. CHANDLER, of London, agreed that phrenic evulsion was seldom advisable. He thought that oleothorax was often useful, especially where obliterative pleurisy was occurring.

DR. W. ANDERSON, of Aberdeen, while admitting that relaxation of the lung was the chief cause of improvement following various surgical procedures thought that other factors, such as rest, accounted for much of the benefit.

DR. GEOFFREY MARSHALL, London, believed that division of long narrow adhesions was important when the patient had improved and the cavity could not be seen with the x-ray. Otherwise such cases were often disappointing later on.

DR. C. PRICE THOMAS, Newbridge, expressed the opinion that too many physicians still relied upon rest and so-called "building-up" therapy. He agreed that division of the adhesions with the cautery should be more often performed. Sometimes contralateral artificial pneumothorax made a cavity larger, due probably to a valve-like obstruction of the bronchus draining it.

MR. HUGH REID and MR. J. B. HUNTER, both of London, claimed that phrenic evulsion should not be too much condemned. It had its uses in carefully selected cases.

DR. GRAVESEN, in closing the discussion, said that there was still a great deal of activity in a collapsed lung. In his opinion phrenic evulsion was a useless procedure.

*The Section of Pharmacology, Therapeutics and Anesthesia.*—The first session was a combined one with the Sections of Physiology and Biochemistry and Pathology and Anatomy, and consisted in various laboratory demonstrations. Many of the methods were of purely scientific interest but several had a practical bearing. Several useful pieces of apparatus were shown

for the easy administration of oxygen, and DRs. MARRIOTT and KEKwick demonstrated a simple mechanism for the slow transfusion of large quantities of blood by the "drip" method. DRs. CARLETON and LIDDELL, of Oxford, exhibited cats in which the exteriorized artery was available for taking blood pressure. "A meat diet produced a placid animal with a low blood pressure; milk, a hungry animal with a high blood pressure". This unlooked-for result shows how careful we must be in applying animal experimental results to man.

The second session was devoted to the discussion of "Cyclopropane anesthesia" in the first place, and then went on to discuss "Anesthesia in labour". During the whole session the Section combined with that of Obstetrics and Gynaecology.

DR. RALPH WATERS, Madison, U.S.A., opened the discussion on cyclopropane by suggesting a new process of manufacture of the gas which much reduced the cost. This anaesthetic caused no respiratory stimulation, but on the contrary a slight depression. The pulse should be carefully watched because there was a risk of ventricular fibrillation. This was apt to be preceded by a very slow heart. The post-operative respiratory complications were definitely less than with other anaesthetics. The use of the drug was still in the experimental stage and much has yet to be learned about it.

DR. DIVINE, of Hull, in an experience with 92 cases, said that he had seen both bradycardia and arrhythmia under its use.

DR. SIMMONS, Bournemouth, recorded a death from its use in which ventricular fibrillation was noted. Several other speakers gave their experience with the gas which was far from encouraging.

The discussion on "Anesthesia in labour" brought out many differences of opinion, both as to the drugs to be used and as to the time and the methods of employing them.

MR. L. C. RIVETT said that two trained persons should always be present at every labour,—surely a counsel of perfection!

DR. FEATHERSTONE, of Birmingham, remarked that if the patient was to be rendered unconscious (*i.e.*, anesthesia induced) then this should be done by one practitioner, leaving the other free for necessary manipulations. Most speakers thought that chloroform was on the whole the best anaesthetic during labour, but should not be used too early. According to DR. HELEN E. RODWAY it was unwise to use any drugs for the relief of pain until the uterine contractions were well established, and inhalation anesthesia should be reserved for the second stage.

DR. R. J. MINNITT, Liverpool, called attention to the difference between analgesia and anesthesia, and believed that the former is all that is usually necessary.

DR. Z. MENNELL, the final speaker in the symposium, was in favour of the proper use of chloroform both as an analgesic and as an anaesthetic.

The social part of the gatherings of the British Medical Association is always a strong feature and the Oxford meeting excelled itself in this respect. There were many lunches and dinners, receptions and garden parties. Even special breakfasts were held on several mornings. There was much dancing and golf for the active, and a chess tournament had been planned but no time could be spared for it. One particularly enjoyable garden party was given by MR. H. S. SOUTTAR for those who had been overseas to the Melbourne meeting. DR. DOUGLAS, the oldest member of our party, was there and was congratulated on being elected a vice-president of the Association.

LORD NUFFIELD had several parties out to see the Morris car works, and we there saw the marvellous way in which these cars were assembled and turned out at the rate of 500 a day.

Of Oxford I will say little, as it is so well

known. The town reeks of antiquity, and yet in many ways is thoroughly up-to-date. MR. SOUTTAR's house is over four hundred years old.

On one evening the mayor held a reception in the Town Hall. The mayor is a lady, COUNCILLOR MRS. TOWNSEND, and very well she discharges her duties, and at the annual banquet made a charming speech. In many English towns and cities, as in Oxford, the Councillors are the lower rank of city fathers, and the aldermen the higher, and the latter hold their appointments for life, while the Councillors are elected every three or four years. The mayor is appointed annually.

On Friday evening DR. R. R. MARETT gave the annual popular lecture, which was largely attended. His subject was "Anthropology and medicine", and he spoke in the old Sheldonian Theatre.

On Saturday there were several garden parties, but most of the members had scattered to their homes, all doubtless bearing away with them many happy memories of a most successful meeting, and probably having the best of intentions of meeting again in Belfast next July.

## Men and Books

### THE DAWN OF TROPICAL MEDICINE\*

BEING A BRIEF ACCOUNT OF THE LIFE AND  
WORK OF SIR PATRICK MANSON

BY P. MANSON-BAHR, D.S.O., M.D.,  
F.R.C.P., D.T.M. & H.

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No attempt is made here to claim that Manson discovered Tropical Medicine, but emphasis must be laid on the fact that by his work and precepts he made it a new and living thing; that he was the first to elucidate the cause and transference of many hitherto obscure tropical diseases; that as a great clinician he transformed the specific treatment of these diseases; and that, most certainly, he was the first to found and direct a school devoted to the teaching of tropical medicine and thereby to render safe for colonization and development many unhealthy and inhospitable countries in the British Empire and other parts of the tropics. Indeed the benign influence of his discoveries, of his example and of his life, is world-wide.

Of pure Scotch parentage, though descended originally, as he often jocularly remarked, from Norwegian pirates, Manson was born in humble

circumstances in the ancient town of Old Mel-drum, Aberdeenshire, on the 3rd October, 1844. His earlier years were spent in training at the gymnasium of Aberdeen city for the engineering profession, a training which in originality of method and dexterity in execution afterwards stood him in good stead. However, the Fates ruled otherwise, for, at the early age of sixteen, he developed a curvature of the spine for which he had to rest for six months and it was during this period that he decided to enter the medical profession. Neither at school nor at the university did he display any particular brilliancy, but he was a steady hard-working student. He, however, made such headway that by the age of twenty, in 1864, he had passed his final examinations. In 1865 he held the position of Medical Officer to the Durham Lunatic Asylum, making a series of careful dissections of the brains of the insane, and he published an article on minute aneurysmal dilatations of the cerebral arteries which he maintained were the cause of mental disease. In 1866 he "fared foreign", and in the autumn of that year landed at Takao on the southern shores of Formosa, where he spent the next four years. In 1870 he moved to Amoy, a "treaty port" on the mainland of China in the Bay of Hiu Tau, where he worked more or less in obscurity till 1875.

Amoy was typical of a Chinese city in those days — unsanitary, ill-kempt and filthy — just teeming with disease, and here he was led to reflect upon the causation of elephantiasis and leprosy, the two diseases which he mostly en-

\* An address (somewhat abbreviated) delivered at the opening of the 90th course of study at The London School of Hygiene and Tropical Medicine on February 3, 1931.

countered. It is certain that from his peculiar sympathy with the Chinaman, his professional skill, and outstanding personality, he soon gained a moral ascendancy with the people with whom he was brought into contact, to such an extent that he gained their confidence, and was able to perform operations hitherto unheard of in China. We know from his records that in one year he removed with complete success "a ton of elephantoid tissue", besides performing the operation of "cutting for stone", and many upon the eye. Very soon his reputation for surgery, and especially his knowledge of eye diseases, resounded all over China. In midwifery he appears to have been no less successful, and to those familiar with the conservative disposition of the Chinese this in itself is very remarkable.

Returning to England in 1875, he busied himself in museums, medical schools and libraries, endeavouring to find out more about the diseases in which he was so deeply interested, but he could find little literature and no authorities on the subject and his enthusiasm received no encouragement. At last one day, in the autumn of 1875, he found amidst the dusty precincts of the reading room of the British Museum the writings of one Timothy Lewis, a very distinguished officer of the Army Medical Service in India. In 1870 this Lewis had discovered certain nematode worms in the blood of natives of Calcutta which he had named the *Filaria sanguinis hominis*—the threadworm of the blood of man. Manson instantly seized upon the idea that these worms might be the cause of elephantiasis, as well as of many other diseases he had observed in Amoy.

The close of 1875 saw him returning to China, provided with a wife and a compound microscope, and fired with many new ideas. Immediately on arrival he set to work to look for the *Filaria* amongst the blood of his Chinese patients in his primitive hospital, which was a rough two-storied Chinese house in Amoy. To aid him in his researches he enlisted the services of two local Chinese assistants, and he soon noted that the more assiduous and the one who worked in the hospital wards late at night was successful in bringing him slides containing the microscopic parasites. A lesser man, or one endowed with a less enquiring mind, might not have noted this discrepancy, but it instantly occurred to him whether this fortuitous occurrence might not be due to the entry of the *Filaria* into the bloodstream at *night time only*; and so it proved to be, for after six weeks' intensive study on one Chinaman (Huito, who should go down to fame) he discovered that his suspicions were indeed correct. The worms appeared in the blood at night time only, but disappeared completely during the hours of daylight. This was indeed a puzzling fact, and when, in 1877, his researches were related at a meeting of the Linnæan Society of London, one sceptic present wished to know whether nature had provided the blood filariae "with watches". Later it was discovered that

when the habits of the patient were reversed, those of his parasite followed suit. So that by sleeping in the daytime and remaining awake at night the filariae could be found in swarms in the day blood, but not at night. On making minute observations upon the filariae removed from the blood and studied under the microscope, Manson had little difficulty in concluding from their structure that they were embryos or the immature state of a much bigger parent worm which, he concluded, must inhabit some tissues of the human body.

This was proved to be true in December, 1876, when Bancroft, in Brisbane, Australia, discovered the adult worm—a long filamentous hair-like creature—almost two inches in length, which inhabited, as male and female individuals, the lymphatic tissues. Now Manson's blood filaria was a much smaller creature, only 1/80th of an inch in length; it was encased, he found, in a loose sheath, in which it struggled aimlessly—tied down as it were, like a man in a sack. The embryo itself had no organs of alimentation, being neither provided with a mouth, an anal pore, or a digestive canal. It seemed to him that nature had provided this small creature with a sheath for some special purpose, for when the blood was cooled outside the body the minute filaria was seen to rupture through its sheath and swim rapidly about in the blood like an active eel. He argued too that the embryos could not possibly develop to any further stage in the blood in which they were being swept along like so many inanimate objects—for did they do so in such countless millions—then the human host himself, like Herod of old, would be entirely "eaten of worms". So he argued that some agent must be necessary for the transference of the filaria from one human being to another and for the development of the parasite outside the human body. It must be a winged agent—something that was nurtured on human blood and something that fed at night time only. What other could that be than a mosquito?

Now the common brown mosquito of Amoy bit at night time only, and was very numerous in the native quarters. So in August, 1877, Manson induced Huito—his filaria-infected Chinaman—to sleep in a mosquito cage and to allow himself to be freely bitten by those insects. The next morning the insects were collected in separately labelled bottles, when engorged with blood, and were kept alive as long as possible. It was not possible to do so for longer than five days, and by dissecting them at frequent intervals with such a primitive instrument as a pen-point Manson soon realized that he had "stumbled upon an important fact with a distinct bearing upon human pathology". For he witnessed a most remarkable fact—the migration of the embryo-filaria, having cast its sheath in the stomach contents, through the walls of the viscera into the muscles of the wings where it developed rapidly into a much larger worm-like creature. "I followed it up," he says, "as best I could with

the meagre appliances at my disposal, after many months of work, often following up false scents, and ultimately succeeded in tracing the filaria through the stomach wall into the abdominal cavity and then into the thoracic muscles of the mosquito. Manifestly it was on the road to a new human host." The idea that a winged insect was the disseminator of disease germs, and that it was an essential link in the development of these parasites, without whose agency it would cease entirely to exist, was a new and startling fact in medicine and, in fact, in biology.

In August, 1878, Manson's paper on the development of the *Filaria sanguinis hominis* and on the mosquito, considered as a nurse, was published in the *Transactions of the Linnean Society of London* and was received with consternation, tinged with scepticism. It proved to be the corner-stone of what is now known as Tropical Medicine, and henceforward Manson had every right to be regarded as a famous man; but in his modesty—for with all his greatness Manson was essentially modest—we find him writing to Cobbold, the greatest extant authority on these matters—"Men like myself in general practice are but poor and slow investigators, crippled as we are with the necessity of making our daily bread."

One of the greatest stumbling blocks to the advancement of knowledge in China was the very great difficulty, or impossibility, of examining the body after death. Only twice did Manson, at great personal risk, undertake this disagreeable but essential task. In both instances he made remarkable discoveries. In the first he found the adult *Filaria bancrofti*, thus confirming Bancroft's original discovery, and on the second occasion he found some ribbon-like worms which proved new to science, and have since been proved to be the immature stages of a big tapeworm. Being denied the opportunity of necropsies in man, he had recourse to dogs, cats and birds of various kinds. In these he discovered a whole host of new parasites, many of them blood worms like the filaria of man, from which he deduced important facts concerning their habitat and mode of life, and which he applied to the parasites of man.

One day a Chinese mandarin entered his room and very rudely and insultingly spat on the floor. "My indignation," says Manson, "evaporated on seeing that the sputum was tinged with blood". So, seizing some with the forceps he immediately placed it under the microscope, and there he recognized the eggs of a strange and hitherto undiscovered worm. It turned out to be the lung fluke—*Paragonimus*—the extraordinary life-history of which he afterwards helped to elucidate. For we know that the eggs of this fluke hatch in water into a motile creature which first enters a fresh water snail and then a fresh water crab in order to get back once more into the lungs of man!

About this time too Manson discovered quite independently, almost simultaneously with Hansen (1879), the leprosy bacillus which he expressed

from lepromous juice. It must be remembered that when summing up the remarkable discoveries that he was working absolutely isolated from contact with other scientists or authorities and cut off from museums and libraries. The idea of this isolation, which must be felt to be realized, makes his achievements all the more remarkable.

In 1889 Manson retired to Scotland. He had amassed considerable wealth, and after twenty-three years in China he had become a famous man, and felt disposed to disport himself in the bounteous woods and waters of his native Aberdeenshire. However, within a year, owing to family misfortunes and the disappreciation of the Chinese dollar which occurred at this moment, he was compelled to try his luck as a consultant in London. Thither he repaired to live many lean and, from the material sense, unprofitable years at 21 Queen Anne Street, Cavendish Square. But soon he found fresh fields for exploration. In blood specimens sent to him from various tropical countries he found no less than four new blood filaria in man—one of which from West Africa—*Filaria loa*—proved the absolute antithesis of his original *Filaria bancrofti*, in that it appeared in the blood stream in day time only, disappearing in the hours of night. His hypothesis, founded on native tradition, that it was carried by a day-biting "mangrove fly" was proved to be correct nearly 24 years afterwards. Here in a small room at the top of the house, euphoniously dubbed the "muck room", he worked out the life history of the guinea worm in the water flea (*Cyclops*), made frequent observations on many other parasites, and predicted their life history in every case, almost with prophetic accuracy. This small room proved to be the nucleus of the future London School of Tropical Medicine. In 1892 Manson made a great step forward in the medical life of London, for he became physician to the Seamen's Hospital Society, a position which gave him ample material for study and practice in the hospitals in the London Docks, under the service of this great Corporation. Here he first began to work seriously with the malaria parasite. By means of a new stain (borax methylene blue) of his own composition, he was able to advance knowledge of the minute structure of this microorganism beyond any hitherto known. He watched the antics of this parasite in blood withdrawn from the body in much the same way as he had observed the filaria in China almost twenty years before. From these pregnant observations, which have never since been seriously challenged, he was able to make suggestive hypotheses upon the dissemination of this disease—"Malaria—bad air—which has so far been popularly ascribed to miasma or emanations from the marshes". So that, in December, 1894, he was able to summarize his knowledge and to publish what is known as *Manson's Malaria-Mosquito Theory*. Briefly this theory compared the life story of the filaria parasite to the supposed life history of the malaria organism, and demanded that a stage

outside the human blood must be passed within the body of a special kind of mosquito found in those tropical countries where malaria abounded. Manson himself approached the Royal Society for a modest grant of £300, to enable him to proceed to British Guiana to work out his project there, which he could not do with very limited material in the cold and dusty atmosphere of his "muck room". Shame be it said that this request was refused! Earlier in that year he had become acquainted with Surgeon-Major Ronald Ross, who had returned from India, where he had interested himself in malaria and had written several papers on the subject. But Ross had not recognized the malaria parasite under the microscope and this, as well as much other technique which he had mastered, Manson set out to teach him.

In 1895 Ross returned to India, inspired by Manson's hypothesis and precepts, and supported by Manson's great authority with the government in England. The years 1895-1899 constituted a period of great activity in malaria research. In this then two great men were closely associated. Indeed there has never been such a close scientific collaboration, and it culminated, as all the world now knows, in the complete vindication of the theory of "Mosquito Manson", as he was then known, worked out to finality by the undying enthusiasm, persistence, ingenuity and zeal of Ronald Ross. Thus did Manson in the last days of the last century come into his own and received the long-deferred honour of the Fellowship of the Royal Society; that was the award of the master—that of the pupil, a similar fellowship and the Nobel Prize. History, however, will record its judgment, that without the initial and basic spade work of Manson's filaria days there would have been no mosquito-malaria theory, and we should still have been looking for the malaria parasite, as Ross so incisively puts it, in water or in air!

On April 9, 1922, Manson died. What is one to say of a great life like his? He was alone in his field, was the great original thinker of his time in the special department of medicine. He died full of honours. Greatly distinguished in his career, a lover of children and of animals, honoured an oracle in the school of his own foundation, appreciative of sport and good literature, Manson belongs to the company of those who have "warmed both hands before the Fire of Life". Without Manson, and without his wonderful prophetic hypotheses, it is safe to say that the elucidation of the mystery of yellow fever would have been long delayed, and that no Gorgas would have arisen betimes to guide American energy, wealth and labour to construct that world-marvel of enterprise, the Panama Canal, and no one, it is safe to say, was more appreciative of the part played by Manson than General Gorgas himself.

In scientific work what better maxim could be followed than the precepts laid down by Manson himself:—

"Never refuse to see what you don't want to see, or what may go against your own cherished hypotheses, or against the views of authorities. These are just the clues to follow up, as is also, and emphatically so, the thing you have never heard of or seen before. The thing you cannot get a pigeon-hole for is the finger-point showing the way to discovery."

## THE SEARCH FOR THE WESTERN SEA\*

### A REVIEW

BY ALBERT G. NICHOLLS,  
*Montreal*

"The Call of the West" has been from the beginning a vital factor in the exploration of America. Mr. Burpee styles it "The spirit of adventure of a vigorous people acting upon a deep-rooted racial tendency to follow the path of the Sun". A thousand years ago the Northmen heard the call and responded to it, thereby discovering a new continent. Nearly four and a half centuries later America was rediscovered, by Columbus, and from that time onward we have the entralling tales of exploration associated with the names of the Cabots, Verrazano, Cartier, Hudson, Button, Foxe, Mackenzie and Fraser, to name only some. To find the Western Sea, the pathway to golden Cathay, was the dream of the early British and French explorers; the story of their quest is a golden epic. "The Search for the Western Sea" is the keynote of exploration in northwestern America, and so provides an appropriate title for our author's fascinating story.

It is a remarkable fact which "may not be without significance, that from beginning to end, from Hudson and Cartier to Mackenzie and Fraser, the men who were engaged in this long search for the Western Sea were for the most part men of Brittany and Normandy, of Scotland and the coast towns of England, legitimate descendants of those hardy Vikings who first of white men set foot on American soil". It is also not without fitness that the expedition that first succeeded in reaching the shore of the Pacific overland consisted of a party of French-Canadian *voyageurs* under the leadership of a Scottish-Canadian.

Mr. Lawrence J. Burpee, is one of the best known of Canadian litterateurs. He has been for twenty-five years Secretary for Canada of the International Joint Commission. He organized and was for several years president of the Canadian Historical Association. He has also been president of the Canadian Authors' Association. He is the editor of the *Journal of the Canadian Geographical Society*. He has been awarded medals by the Royal Society of Canada

\* "The Search for the Western Sea: the Story of the Exploration of Northwestern America." Lawrence J. Burpee. Two volumes; 1,609 pp.; illustrated. New and revised edition. Price, \$10.00. On sale at Dora Hood's Book Room, 720 Spadina Avenue, Toronto.

and the French Academy for his outstanding work in Canadian historical research. He is the president of the Royal Society of Canada. There can, therefore, be no question as to his competence for the task he has undertaken.

"The Search for the Western Sea" was first published in 1908 and at once established itself as the authority on the exploration of northwestern America. This first edition is now rare and expensive. Since this date much new matter has come to hand through the researches of many scholars, and documents acquired since by the Dominion Archives have thrown new light on the character and achievements of the early explorers in Canada. The present volumes, therefore, can be accepted as a great advance on the original work.

Mr. Burpee gives some space to the pioneer discoverers, Leif Ericson, Columbus, Verrazano, the Cabots, and Jacques Cartier, but expends his talents on the more modern period, on such men as Hudson, James, Hearne, La Vérendrye and his sons, on Carver, Pond, Mackenzie, Simon Fraser and David Thompson. His narrative practically closes with Mackenzie's overland expedition to the Pacific, Fraser's descent of the Fraser River, and Thompson's exploration of the Columbia, the accounts of these being graphically told. The hitherto uninitiated reader will find it a little complicated to follow the innumerable geographical details of the story, but the subject is much clarified by the presence of an excellent introduction.

Western and northwestern Canada is studded with countless lakes and intersected by many winding rivers. By means of portages the early explorers, aided or hindered, as the case might be, by the reports and activities of the Indians, eventually made their way southward, northward, and westward by the waterways, but the going was hard and tedious, as the rivers were often long and tumultuous. One wonders at the learning and patience of our author which have enabled him to present the intricate matter of the geography of this part of Canada and its bearing on the travels of the pioneer explorers in such a clear way. The task was great; it has been admirably performed. Details which might have proved boring are lightened by anecdote, personal sketches of the actors in the drama, and accounts of the various Indian tribes with whom the wanderers came in contact. The result is a gripping and informative tale.

The subject is dealt with systematically under three headings—"The Northern Gateway", "The Southern Gateway", and "The Road to the Sea".

The northern gateway is Hudson Bay. In this section of the book we have an account of the discovery of Hudson Strait (by an unknown before 1508), by the Portuguese (?1558 to 1570), and by Davis (1587), and a fuller account of Hudson's voyage, with its disastrous ending. The search for the "Northwest Passage", how-

ever, still continued, and we learn about the expeditions of Sir Thomas Button, Jens Munk, and Captains Luke Foxe and Thomas James. We are informed of the interesting fact that the "Strange and Dangerous Voyage" of Captain James formed one of the main sources, if not the main source, of Coleridge's "Ancient Mariner". Then follows the first voyage of Chouart and Gillam on the *Nonsuch* in 1668, on behalf of a group of men who two years later formed themselves into The Company of Adventurers of England trading into Hudson's Bay, commonly called the Hudson's Bay Company. On this occasion Chouart and Gillam established Fort Charles on James Bay, the first trading post of the Company, and thus initiated an enterprise that has flourished up to the present day.

Next comes the story of the first authenticated journey from Hudson Bay to the upper Saskatchewan River—that of Anthony Hendry (1754-55), which is followed by a graphic account of Hearne's discovery of the Coppermine, the massacre of the Eskimos at Bloody Falls, and the surrender of Fort Prince of Wales to Admiral LaPerouse under circumstances savouring of opera bouffe. The chapter closes with the names of Philip Turnor, Peter Fidler and David Thompson. Hearne's travels are important as they settled finally in the negative the question as to whether there was or was not a "Northwest Passage" by way of Hudson Bay.

If the northern gateway was preeminently the portal by which the English adventurers entered the unknown land, the southern gateway, that by way of the St. Lawrence valley and the Great Lakes, was equally associated with the French. Two hundred years of exploration had opened up this tract of country as far west as the height of land that separates the waters flowing east to the Gulf of St. Lawrence from those that flow north of Hudson Bay and south to the Gulf of Mexico. Burpee credits Radisson and Chouart with being the first to connect Lake Superior with Hudson Bay by an overland expedition (1662). The great heroes in the epic are Pierre Gaultier de La Vérendrye and his three sons. In the face of much opposition and adverse circumstances these heroic men discovered Lakes Winnipeg, Manitoba, Winnipegososis, some of the upper reaches of the Saskatchewan River, and traced the Missouri as far as the foot-hills of the Rocky Mountains (about 1743). After the conquest of Canada numerous attempts were made by the English to realize the dream of the French, to blaze a trail to the Western Sea, the first of which was that of Jonathan Carver (1766-68) who left an account of his wanderings in his "Travels through the Interior Parts of North America", an entertaining though somewhat untrustworthy production.

The second volume is, if possible, more delightful than the first. In it we have the fruition of the hopes of the long line of intrepid explorers who brought honour to the French and English races. The Western Sea is discovered by path-

ways from the east. We learn something of the operations of that second great trading concern, the North-West Company, which had its headquarters in Montreal and became such a formidable competitor of the older Hudson's Bay Company. The rivalry between the two became intense, finally culminating in bloodshed. Then, commonsense prevailed and the two companies amalgamated. We are brought face to face with James Finlay, of Montreal, who, not later than 1767, reached the Saskatchewan, and with Alexander Henry the elder, who in 1775 reached the Grand Portage, Lake Winnipeg, Saskatchewan River, and Ile à la Crosse. Other noted figures of the time are Peter Pond, Joseph and Thomas Frobisher, Roderick Mackenzie, C. J. B. Chaboillez, and Simon McTavish.

The remarkable travels of Alexander Mackenzie, Simon Fraser and David Thompson are dealt with at length and form the most dramatic portion of the book. The resourcefulness, skill and determination of these great men are almost unbelievable. Posterity owes them much.

Mackenzie discovered the mouth of the great river named after him, tracing various sections of its course at different times, and eventually stood at one of its remote sources two thousand four hundred and twenty miles up stream. He was the first of the overland explorers to stand on the shores of the Pacific. He travelled up the Peace River, up its tributary, the Parsnip, and by a portage and some intervening waters reached the Fraser River, emerging at the sea somewhere near the present Bella Coola. This was in 1793.

Simon Fraser discovered the Fraser River and descended it almost to its mouth, reaching a point near where the city of New Westminster now stands. Fraser at the time thought he was on the Columbia River and Thompson was paddling up the Columbia without realizing it. This was not surprising!

Thompson reached the source of this river in Upper Columbia Lake in 1808, and in about three years had traced its course from source to mouth, a distance of eleven hundred and fifty miles. Dr. Coues pays Thompson this fine tribute—"The world can never be allowed to forget the discoverer of the sources of the Columbia, the first white man who ever voyaged on the upper reaches and main upper tributaries of that mighty river, the path-finder of more than one way across the Continental Divide from Saskatchewan and Athabaskan to Columbian waters, the greatest geographer of his day in British America, and maker of what was then by far its greatest map." Thompson, we understand, has also another title to fame worthy of note, in that he was the surveyor who laid out the principal streets of Montreal. In his old age he fell on evil days, dying in poverty on February 16th, 1857, at the age of nearly eighty-seven years. Three months later his wife followed him. They are buried

in Mount Royal Cemetery, Montreal. The book closes with an appreciative account of the many notable men connected with the Geological Survey of Canada whose work has done so much to fill in the gaps in the geographical record left by their predecessors—Robert Bell, George M. Dawson, A. P. Bell, the Tyrrells, and others who might be mentioned. Even yet much remains to be done, but the aeroplane is with us, and surveys and observations can now be made in days, where formerly they took years.

We could have wished to get more information on medical topics, but, no doubt, these had no special interest for Mr. Burpee. We wonder whether the various explorers in our Canadian North-west had medical men with them. Possibly the early expeditions by ship into Hudson Bay had their doctors, but we are not told. The French sometimes took medical men along with them. We know, for instance, that LaSalle, when he went on his famous voyage down the Mississippi (1678-83), had two with him—Jean Michel and Jean Roucel.

There are sundry statements which lead us to infer that scurvy took the usual toll that was so exacting in those early days. The white men were, on one occasion at least, specifically blamed by the Indians for introducing smallpox.

An interesting anecdote is told on page 485 in which Alexander Mackenzie figures. The son of the old chief of the Coast Indians was suffering from an ulcer. The white chief was requested to touch the sick man and make him well. This was somewhat disconcerting, and Mackenzie had recourse to an old stand-by—Turlington's Balsam. The effects not being immediately apparent the native doctors again took charge. They blew on the unhappy patient and then whistled; they rubbed him violently on the stomach; they thrust their fingers into his mouth, and spouted water into his face. He was then carried on a plank into the woods, where a fire was kindled, and the ulcer was treated heroically by cauterization with red hot instruments. We are told that the scene was too much for Mackenzie, who hastily withdrew.

There is an interesting reference to Dr. John Coakley Lettsom, the celebrated Quaker physician who founded the Medical Society of London (1773), and in whose memory the Lettsomian Lectures were instituted. The "Travels" of Jonathan Carver, according to Professor Bourne, "can no longer be ranked as an authentic record of the observations of the supposed author", and he conjectures that in its present form this record is the work of Lettsom, who wrote much and was the charitable friend of Carver. It is assumed that Lettsom prepared the book from Carver's notes and recollections of his journey, and padded it out with unacknowledged extracts from French journals and histories of New France. Commenting on this, Burpee adds,—"Admitting the

correctness of Professor Bourne's conclusions, it is singular that a book so cobbled together could have inspired two such masterpieces as Chateaubriand's 'Voyage en Amérique' and Schiller's 'Nadowessiers Todtenlied', later translated by Bulwer-Lytton as 'The Indian Death-Dirge.'

This imperfect sketch will give some indication of the character of Mr. Burpee's book. Those who take an interest in the early exploration of our country will find in it a rare treat.

## Hospital Service Department Notes

### Major and Minor Operations

Enquiries are frequently made as to how these two groups can be differentiated and a perusal of the literature makes it soon evident that definitions differ widely. For instance, the description of a major operation as one that involves the risk of a life might require almost all operations to be considered as major ones, for, in almost all, when done under certain circumstances, there is possible danger to life. In an illuminating discussion of this subject, the Editor of the *Canadian Hospital Journal* reviews various attempts to clarify this differentiation.

A definition given by the American Medical Association considers as major "surgery within the cranial, thoracic or abdominal cavity, or any surgery which, through the nature of the operation or the anaesthetic demanded, may carry a distinct menace to life". Dr. S. S. Goldwater, of New York, states that "a major operation is a severe or serious operation, not a slight or trivial one, but from comparatively trivial surgical procedures serious consequences sometimes result. The test lies in the gravity of the operation, which must be gauged not merely by the technical difficulty of the procedure but by the risk to the patient . . . . Elements to be considered are—the scope of the surgical procedure; the danger of shock; the presence of known complications; the probability or possibility of unsuspected pre-existing surgical complications; the probability and possibility of post-operative complications; the probable duration of the operation; the age and general condition of the patient; the degree of mutilation; the amount of pain or mental anguish caused; the nature of the anaesthetic; and the risk of legal complications in the case of an unsuccessful result."

All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 184 College Street, Toronto.

Dr. M. T. MacEachern, of the American College of Surgeons, has stated that "the best definition . . . is that which we received from the American Medical Association, which states that a major operation is a surgical procedure that entails immediate serious consequences to the patient and requires skill and training to perform". Dr. Nathaniel W. Faxon, of Boston, who, like the two authorities quoted above is also a former president of the American Hospital Association, after reviewing various factors, says "The most important factors in defining major and minor surgery are: 'Whether the patient remains ambulatory, whether a general anaesthetic has been given and the risk for the patient'. He points out that many infections of the hand, formerly regarded as of a minor nature, are now considered as requiring major procedures because of the economic value of a functioning hand.

In summing up the various opinions the Editor notes that the differentiation is usually based upon factors associated with the patient, and makes the suggestion that certain simplification would be forthcoming if the *skill of the surgeon* were made the deciding factor, as an operation may be minor when done by a skilled surgeon but would be of major nature, because highly dangerous to the patient, if performed by an inexperienced or ill-trained surgeon. Reference is made to the procedure in one well-organized hospital where a full list of operations is divided on the basis of the rank of the surgeon who may do them. For instance, brain surgery, open bone work, gastric and gall-bladder surgery, all internal malignant conditions, splenectomy and post-operative herniotomies *inter alia* may be done only by the senior major surgeon; empyema, rib-resections, trachelorrhaphy, non-ruptured appendicectomies and inguinal herniotomies, among others, may be done by the junior major surgeon; the latter may only do benign breast tumours, umbilical hernias, uterine suspensions or ovarian cysts, after consultation with the senior major surgeon. The minor surgeon may do tonsillectomies, transfusions, diagnostic biopsies, finger and toe amputations, emergency tendon- and nerve-suturing, and other listed and obviously minor procedures.

This basis has the advantage of giving the patient assurance of competence on the part of the surgeon officiating. From a practical viewpoint one questions to what extent it could be adopted by our hospital staffs. In highly organized and departmentalized hospitals there should be very little difficulty, particularly with reference to ward or staff patients, but in the majority of our hospitals (and there are more under fifty beds capacity than over) the surgical work is done by a small handful of men, all of whom are usually in general practice as well and

usually on an equal footing in the hospital organization. In such smaller institutions it would be difficult for the staff to determine to what extent each of the local surgeons would operate. However, no matter how small the hospital (excepting perhaps isolated one-doctor hospitals) the staff could readily adopt the suggestion of listing certain operations which they would mutually agree would not be attempted (barring emergency situations) except after consultation and with certain qualified assistance.

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## Provincial Association Notes

### The Nova Scotia Medical Society

Reiterating its approval of unification of the Canadian Medical Association with the provincial societies, the Nova Scotia Medical Society met in annual conclave at Halifax, August 31st to September 5th. The meeting was concurrent with the Dalhousie Refresher Course which took care of the scientific part of the program. The business sessions of the society were well attended and registration the largest in many years.

Outstanding at the first meeting was the report of the special committee appointed to consider amalgamation with the Canadian Medical Association. The report warmly approved of the motive and principle of unification. It was felt that the problem was a great one and that every step should be carefully planned and checked in advance. It was further pointed out that the Nova Scotia Medical Society is under special charter of the Nova Scotia government and is not free to dissolve itself or alter its status. The report recommended further investigation of the plan and cooperation with it, and advised consultation with the department of the Provincial Attorney General. The report was adopted.

Dr. K. M. Robertson, President of the Canadian Association, and Dr. T. C. Routley were welcome guests at the banquet and meetings where they spoke on the work of the Association.

Sterilization of the mentally unfit was the problem which Dr. R. M. Benvie, retiring president of the society, served with the coffee at the annual banquet. Dr. Benvie, who occupied the chair with justice and grace throughout the sessions, gave a presidential address which gratified both those who sought learning and entertainment. Presenting the modern conception of embryology with reference to inherited characteristics, he established reasons for the increase of mental defectives in Canada. They cost the people of Canada twelve

million dollars yearly, nor is this the most serious aspect of the tragedy. It would take three thousand years to reduce the incidence, by sterilization, to one per thousand. This, Dr. Benvie felt, was good reason for the immediate legalizing of sterilization. He urged on the profession the importance of preaching the doctrines of eugenics and heredity to the laity.

Dr. J. R. Corston, of Halifax, was elected President for 1936-37. First Vice-president, Dr. A. Calder, Glace Bay; Second Vice-president, Dr. J. H. L. Simpson, Spring Hill; Secretary, Dr. H. G. Grant, Halifax; Treasurer, Dr. W. L. Muir, Halifax. Study committee on confederation, Dr. K. A. MacKenzie (chairman).

The annual meeting of 1937 will be held at Pictou.

ARTHUR L. MURPHY

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## Medical Societies

### Brandon and District Medical Society and The Northwest Medical Society

A meeting of the Northwest Medical Society and the Brandon and District Medical Society was held at Clear Lake on September 9th, with a large attendance of doctors and their wives, 110 being present at the dinner. Dr. Geo. Clingan, Virden, President of the Manitoba Medical Association, presided. The chief subject of discussion was "Anterior poliomyelitis", and Dr. F. V. Bird, of Boissevain, where the present outbreak began, spoke of the clinical features of the disease and stressed the importance of administering convalescent serum as soon as possible, without waiting for too-well developed symptoms. Dr. C. R. Donovan dealt with the epidemiology. He considered that the protective properties of the nasopharyngeal mucous membranes could be enhanced with a spray of picric acid and sodium alum solution. Dr. N. R. Rawson lauded the value of convalescent serum; and Dr. E. L. Ross, of Ninette Sanatorium, mentioned the value of the respirator in tiding over a patient who had developed respiratory paralysis.

There was also a symposium on "Undulant fever", the speakers being Dr. J. N. Andrew, Minnedosa, Dr. C. R. Donovan, Department of Health, and Dr. N. R. Rawson, Brandon. Dr. G. S. Fahrni, Winnipeg, gave an address on "Upper abdominal pain". At the banquet, held in the main dining room of the chalet, Dr. S. J. S. Peirce, Brandon, spoke on the subject, "The doctor looks at politics". Mrs. George Clingan and Mrs. S. J. S. Peirce acted as hostesses.

Ross MITCHELL

### The Canadian Physiological Society

The Canadian Physiological Society, organized in Toronto in October, 1935, will hold its next meeting at Queen's University in Kingston, October 24th. There will be two scientific sessions, one in the afternoon, and one in the evening. The Society has now a membership of more than 160, and includes scientists from Prince Rupert to Halifax.

### The Edmonton Academy of Medicine

During the past summer months, when regular meetings of the Academy are discontinued, the medical profession of Edmonton and vicinity have been especially favoured by having as visitors to our city several prominent members of the staffs of McGill and Toronto University Medical Faculties. During their short sojourn in the capital of Alberta the following meetings and clinics were arranged to which these distinguished visitors from the East generously contributed highly scientific and helpful addresses on the latest developments in medicine and surgery.

On June 17th, at a special meeting at which 110 members and guests were present, Dr. Duncan Graham, Professor of Medicine at Toronto University, read a paper on "Some problems in the diagnosis and treatment of peripheral arterial disease". He dealt with various aspects of peripheral vascular disease, including arteriosclerosis, thrombo-angiitis obliterans and Raynaud's disease. The paper was discussed by Drs. Pope and Hurlburt. Dr. F. F. Tisdall, Associate Professor of Paediatrics, University of Toronto, also contributed a paper, illustrated by a series of lantern slides, in which he outlined much original, interesting work in nutrition and discussed its clinical application. The paper was discussed by Dr. Leitch.

On July 6th, at a special meeting of the Academy held at the University Hospital, Dr. F. S. Patch gave a bedside clinic at which the following cases were presented: (1) Ruptured urethra; (2) pyonephrosis; (3) tumour of the kidney in a child. Dr. Patch, in an admirable fashion discussed the clinical diagnosis and treatment of these conditions. Following a luncheon, Dr. Patch, the guest speaker, gave an address on "Newer aspects of urology," in which he discussed the following subjects. The speaker outlined the value of trans-urethral resection of the prostate in selected cases and pointed out that it would not completely replace a suprapubic operation. The value of the use of uroselectan in visualizing the kidney pelvis was outlined. The speaker also discussed the newer urinary antiseptics and stated that these agents had a very limited application. He stressed the point that the physician should try to determine the causative factors in urinary infections and remove them. The meeting was

well attended, a number of physicians from outside the city being also present.

On July 9th a largely attended meeting of the Academy took place at the Royal Alexandra Hospital to hear Dr. Roscoe Graham. Dr. Gordon Gray, president, was in the chair. Dr. Graham gave a very interesting clinic on a number of cases, covering various problems of surgical diagnosis and treatment. The speaker's methods of presenting these cases was very much appreciated. Through the courtesy of Dr. Anderson, Medical Superintendent of the Hospital, lunch was served, after which Dr. Graham again addressed the Academy on "Safety factors in abdominal surgery". Dr. Graham's visit was very much enjoyed and he well sustained his reputation as one of the outstanding teachers and clinicians in America.

T. H. WHITELAW.

### The Peace River District Medical Association

The Annual Meeting of the Peace River District Association was held at Dunvegan on August 12th, 1936, when the following visitors were present: Dr. Fulton Gillespie, of Edmonton, President-Elect of the Alberta Division, the Canadian Medical Association; Dr. F. J. Folinsbee, of Edmonton; Mr. W. G. Hunt, Calgary, Associate Secretary, the Alberta Division, the Canadian Medical Association.

A discussion of the question of organized medicine in Canada was led by Dr. Gillespie.

The meeting recommended to the consideration of the Council of the College of Physicians and Surgeons, that a new electoral constituency for the Council be established for the Peace River District. The old officers were re-elected.

Following the discussion Dr. Gillespie read a paper on "Rectal ailments" and Dr. Folinsbee one on "Infant feeding and the deficient child".

A scientific meeting was held on August the 11th at Peace River. Among the members present were Dr. Percy Jackson, from Keg River, about 200 miles north of steel. At this meeting Drs. Gillespie and Folinsbee gave papers.

Camrose District Meeting was held at Camrose in August, the following provincial officers being present: Dr. D. S. Macnab, Calgary, President of the Alberta Division, Canadian Medical Association; also Dr. I. R. Bell, Coronation, who gave a scientific paper.

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It seems an inseparable accompaniment of the advancement of knowledge that things once thought to be units turn out to be composites; the magic prism of investigation is always splitting up apparent entities into an ever-increasing number of new elements.—E. O. Jordan, *J. Prev. Med.*, 1929, 3: 279.

## Post-Graduate Courses

### The Montreal Medico-Chirurgical Society

The Montreal Medico-Chirurgical Society will hold its Fourth Annual Clinical Convention in conjunction with the Reunion of Graduates of McGill University, on October 21 to 24, 1936.

Interesting and varied clinical sessions are being planned by the Program Committee. These sessions will be held in the Royal Victoria Hospital, the Montreal General Hospital, the Royal Victoria Montreal Maternity Hospital, the Children's Memorial Hospital, and McGill University, and will run continuously on the above dates as follows:

*Wednesday, October 21st.—All day. Montreal General Hospital.*

*Thursday, October 22nd.—Morning. Children's Memorial Hospital.*

*Friday, October 23rd.—All day. Royal Victoria Hospital.*

*Saturday, October 24th.—Morning. Royal Victoria Montreal Maternity Hospital.*

## University Notes

### Dalhousie University

The Dalhousie Medical School resumed classes with what will probably prove to be the largest enrolment in its history. First year registration stands at 60, of whom 50 are from the Maritime provinces. The primary purpose of a university is the education of its own people and so large a local representation is gratifying to the faculty.

Newly appointed to the chair of Physiology is Dr. Charles B. Weld, a 1929 graduate in medicine of Toronto University. Dr. Weld took his Arts degree at the University of British Columbia, where he also became a Master of Arts in bacteriology. Since 1922 he has spent much time in research, both in bacteriology and physiology. During the summers of 1926 and 1927 he was attached to the Marine Biology Station at Halifax. He interned at the Toronto General in 1929-30 and has been a Research Associate at Toronto University since, while carrying on a general practice in the city. In 1935-36 he was Assistant Professor of Physiology. His brilliant scholastic record, tempered by his years as a general practitioner, fits him well for his new position.

ARTHUR L. MURPHY

## Special Correspondence

### The London Letter

(From our own correspondent)

When all the institutions administered under the old "Poor Law" were transferred to the municipal and county council health authorities some years ago one of the stipulations, of a more or less permissive nature, was to the effect that close cooperation between the voluntary hospitals should be a matter of policy. So far this has not by any means been universally carried out, although in some cities (*e.g.*, Manchester) a definite joint hospital policy has been formulated. Recently an accident case in Kent, many miles from London, was actually transported to Guy's Hospital because all the local voluntary hospitals were full and yet as subsequently transpired the local county hospital, near to the scene of the accident, could easily have admitted the injured patient. It has been estimated that the larger teaching hospitals in Great Britain have a waiting list which averages about 1,000 patients per institution and such patients could probably be accommodated without much difficulty if the municipal hospitals were properly used. It cannot be economically sound to keep working men and women waiting for cure of such conditions as hernia, and the modern accident problem tends to flood the teaching hospitals with emergency cases which might well go elsewhere. A special Voluntary Hospitals Commission is at present in session to try and secure some common policy, but what appears to be wanted is a wider survey of the whole hospital field, in order that the total beds available in whatever institution can be best rendered available for those who require them.

Last month Sir Herbert Barker demonstrated his manipulative methods before a special meeting of the British Orthopaedic Association. This simple statement contains much of historic interest, for it recalls the controversies of past years when the famous bone-setter was the object of much popular sympathy, some of it as much misplaced as it was foolish. At the demonstration various patients received the special forms of treatment which Sir Herbert has himself devised. It is of interest that some of these are frankly empirical, and also that the president emphasized that all the orthopaedic surgeons present now practise manipulation. Among the new appointments to His Majesty, King Edward VIII announced recently was the new one of "manipulative surgeon" filled, it may be stated with pride, by a medical man.

Medical care in industry has made great strides in the past few years, and the newly formed Association of Industrial Medical Officers now holds four meetings a year of medical men and women who devote the whole of their time to the subject of industrial medicine and hygiene. The September number of *The Practitioner* is devoted

largely to the subject of industrial medicine, suitably introduced by Sir John Simon, the present Home Secretary, who compares the position in industry now with what it was when he held his office twenty years ago. The importance of poisons, of lung disease, of psychological ailments, of skin disorders, and of absenteeism are some of the subjects dealt with by appropriate authorities, while the question of general hygiene and preventive measures receives adequate mention. In this connection the work of the Industrial Health Research Board is of great importance, and a recent report has dealt with conditions of comfort in factories. One of the findings was to the effect that cold air at foot level produces more discomfort than on the other parts of the body. The most comfortable temperature was about 65° F. but "comfort" was found to be experienced under a wide range of conditions. It is stated that part of future experiments planned on this subject is to include a study of the ventilation of the House of Lords, where, presumably, cold feet and hot heads may adversely affect the legislation of the nation!

Outside detective novels the highly trained medical investigator of crime does not exist in this country. There is no standard method of training those who conduct pathological investigations for the police, and indeed the whole subject of forensic medicine is rather the Cinderella of the medical curriculum. The newly-formed Metropolitan Police Laboratory offers certain facilities on a comparatively narrow basis. The Advisory Committee on the Scientific Investigation of Crime recommends unanimously something much wider—an institute with a recognized place in the academic sphere as a school of the University of London in the Faculty of Medicine. A certificate or diploma would be granted after a course of varying length, and on the pathological side there would soon be available a list of men suitable for selection by coroners for the performance of autopsies.

ALAN MONCRIEFF.

121 Harley St.,  
London, W.C.1.

### The Edinburgh Letter

(From our own correspondent)

The Annual Meeting of the British Medical Association held at Oxford under the presidency of Sir Farquhar Buzzard was an outstanding success. The environment further added distinction to the proceedings. The Association has expressed its warm thanks to the Local General Secretary, Dr. F. G. Hobson and his colleague, Dr. H. D. Woodroffe, to the Science Secretary, Dr. A. M. Cooke, and to the Chairman of the Executive Committee, Dr. W. Stobie. It has also expressed its indebtedness to the Vice-Chancellor of the University, to Mrs. Townsend, the Mayor, to Lord Nuffield and to many other persons who gave ungrudgingly of

their time and energy. The representative Meeting was presided over by Mr. H. S. Souttar, and the elder statesmen, in the persons of Dr. E. Kaye Le Fleming the Chairman of Council, Sir Henry Brackenbury and Dr. C. O. Hawthorne, did much to enhance the interest and usefulness of the proceedings. That these proceedings were less controversial than usual is a tribute to the efficient work done by the Council during the year. Dr. W. Paterson, Chairman of the Dominions Committee, in moving approval of the section of the Report dealing with the Oversea Branches said that the representatives would realize that on the work of the members of the Oversea Branches depended the health and happiness of a very large number of the inhabitants of the British Empire, and that a debt was owing to them which could hardly be paid, especially as many of them worked under very trying conditions. Dr. Paterson also expressed the wish of the whole meeting that the forthcoming visit of Dr. G. C. Anderson, the Medical Secretary of the Association, to India would be very pleasant and successful. The Canadian Medical Association was represented by Dr. H. S. Birkett and Dr. A. H. Gordon, both of Montreal, and Dr. R. D. Rudolf, of Toronto. The meeting received with very great pleasure the greetings and good wishes sent by the Canadian Medical Association.

Sir Godfrey Collins, Secretary of State for Scotland, has introduced in the House of Commons the Maternity Services (Scotland) Bill. The main purpose of the Bill is to improve the standard of home midwifery and to secure adequate nursing and medical services for maternity in Scotland. The Bill supplements the existing provisions and envisages a comprehensive maternity service. It places on local authorities a duty to make arrangements for the provision to women in their own homes of the services both of a certified midwife and of a medical practitioner. The scheme provides for (1) medical examination and treatment during pregnancy, (2) medical supervision during the lying-in period, (3) medical examination at least once after the expiry of one month after child-birth, and (4) the services of an obstetrician to advise and assist where necessary. This is in accordance with the recommendations made in the Report of the Committee on Scottish Health Services which stated that "the service should be based on the doctor and midwife in concert, supplemented by consultants and adequate institutional facilities". The principle underlying the Bill is one of which the medical profession generally will heartily approve. It is that supervision of the expectant and nursing mother should normally be part of the family doctor's work. It will also be welcomed by midwives whose status and conditions of work in the past have been far from satisfactory. It is also probable that the reaction of the local authorities to the Bill will

be favourable, since the Bill realizes that different methods may be required in different areas especially with regard to such factors as difficulties of communication and sparseness of population. Further, new Exchequer grants to local authorities will be provided for the service. Provision is also made for preventing unqualified persons from practising as nurses in maternity cases, and for the attendance of midwives at courses of instruction. It is of interest to note that a Midwives Bill has recently been laid before the House of Commons with the object of improving the maternity service in England and Wales. This Bill is much more limited in scope than is the Scottish Bill. At the recent Annual Representative Meeting Sir Henry Brackenbury criticized the provisions of the Bill. He stated that it might be easier for a local authority, having set up a whole-time body of midwives, and having the power to appoint specialists, to use these midwives and specialists for the whole of the maternity work of the locality and exclude the general practitioner altogether. He proceeded to say that the public had been misled, with the best of motives and in complete good faith, by a number of eminent persons on this matter. The public had been led to believe that the maternal mortality of the country was very high and was a disgrace to the nation, whereas, if they compared statistics they would find that maternal mortality in England and Wales was among the lowest of the countries of the world. The public, he added, had also been led to believe that with extra care maternal mortality could be reduced by one-half. That statement required so many explanations and so many qualifications that stated in that crude way it was not true, or else it was meaningless.

R. W. CRAIG.

7 Drumsheugh Gardens,  
Edinburgh.

## Letters, Notes and Queries

### Obstetrics in Equatorial Africa

To the Editor:

Dr. Rabinowitch's account of the Canadian Eskimos was extremely interesting. Practising among a Bantu people of equatorial Africa, I found his account of the birth of a child doubly interesting and a comparison of the two primitive methods may be instructive.

The dating of the obstetrical use of the bedsheet to the Stone Age may be questioned from observations here. Many of the huts here are

Answers to questions appearing in this column should be sent to the Editor, 3640 University Street, Montreal.

built among boulders. Every hut has stones around the fireplace to which the sheets may be tied and plenty of posts to which a tie could be made. But I have never seen or heard of the use of any kind of "pullers". A banana-fibre rope would be thought of in primitive days when all births—as many now—took place in the banana shambe next to each hut. The use of chain "pullers" (made of auto mud chains) in the native hospital was not very popular among the patients nor among the native attendants. The patients much prefer to flex their knees and pull against their own ankles.

The primitive native birth customs here are not very physiological. When labour sets in the woman keeps the information to herself as long as possible, probably to obviate attention from the inevitable mass of villagers who attend the affair. The custom of the old women is to encourage pains and not to let the woman rest between pains. Even in the first stage the woman is encouraged and forced to bear down by beating, holding hands over the nose and mouth, etc. The result frequently is that the patient is tired out before the second stage is passed and those pains are weakened. Then an injection of pituitrin or terminal forceps is extremely useful after she is brought to the hospital.

When left to herself with severe pains the woman will crawl around the banana shambe on her all fours with her pendulous abdomen hanging half a foot below the outlet. The same stunt will take place in the delivery room if she is unwatched.

As with the Eskimos the actual birth takes place in a squatting position. An attendant sits behind the patient and grasps her arms around the patient below the latter's arms and squeezes hard over the fundus. Another attendant squats in front between the patient's legs, and throws cold water over the vulva or plasters it with cow dung, etc., if the labour is too prolonged. The cord is tied with a banana fibre and cut with it or a blade of grass. The baby is dashed over with cold water and laid aside uncovered even if the weather is damp or cool. No attempt is ever made to deliver the placenta. The cord is never pulled on nor the abdomen squeezed. This is inconvenient, as many times we are called for adherent placentas when they would fall out if the woman had merely stood up!

R. B. MICHENER

P.S.—Boys average 7 lbs. and the girls 6 $\frac{3}{4}$  lbs.  
Friends Hospital,  
Kaimosi, P.O. Kisumu,  
Kenya, East Africa.  
August 3, 1936.

### Australasian Medical Congress

*To the Editor:*

Our Executive has instructed us to bring to your notice that the Fifth Session of the Australasian Medical Congress will be held at Adelaide, South Australia, from the 23rd to the 28th of August, 1937. Sir Henry Newland, Adelaide, has been nominated as President.

We have extended an invitation to your President, and also wish to invite any members of your Association who may be visiting Australia to become members of our Congress.

(Signed) ALLAN D. LAMPHIL,  
C. B. SANGSTER,  
*Hon. Joint Secretaries.*

Adelaide, South Australia.

March 19, 1936.

### Hyperhidrosis

*To the Editor:*

How am I to clear up drenching perspiration of a woman of 49 in the menopause? Basal metabolic rate is -25. This woman is well nourished and active. Perspiration will actually soak her dress while you watch. "Pituvarium" of no use. Thyroid extract previously tried elsewhere increases the perspiration.

E. C. H. WINDELER

Windsor, Ontario.

August 1, 1936.

Will some of our readers give suggestions?

[ED.]

### Topics of Current Interest

#### BCG as a Tuberculosis Preventive

There are a number of reasons why the use of the living vaccine known as BCG, twelve years after its first use in France, should still be discussed and debated among those concerned with the prevention and cure of tuberculosis. It has never been conclusively demonstrated that the use of this vaccine is an effective means of preventing human tuberculosis. The reports of studies of its value as an effective vaccine in animals are greatly at variance despite the fact that these studies have been made by excellent investigators. The greatest value of BCG is in cattle but, in view of the variation in reported results, one could scarcely conclude that it is justifiable to use it universally in man. Those who have tried to produce a fixed virus without virulence, using a bile medium by the method of Calmette and Guérin, have failed to do so. Especially notable in this connection

are the studies of A. Stanley Griffith,<sup>1</sup> using seven bovine strains and exactly the method of the French scientists over a period of ten years. Yet he failed to alter the virus.

Since 1900 it has been well known that the injection of certain strains of tubercle bacilli raises the resistance of certain animals to a later killing dose of virulent tubercle bacilli. But the vaccination of man with living tubercle bacilli had never been seriously proposed until 1922, when Professor Calmette enthusiastically suggested it and French physicians began to practise it. This enthusiasm was not shared by British and American physicians, primarily because the determination as to whether it should be used in commerce was in Great Britain in the hands of the Medical Research Council and in the United States in the hands of the National Institute of Health (U. S. Public Health Service) and the Bureau of Animal Industry (Department of Agriculture), which are government agencies. Their conservatism was based on the premise that the ability of the vaccine to justify the claims of the French scientists should be proved by animal tests before employing it wholesale in man.

The enthusiasm with which the French scientists advocated their prophylactic vaccine received a severe blow from the American and British point of view when Prof. Major Greenwood<sup>2</sup> in England criticized the methods of statistical study that were used by Calmette to prove the value of his vaccine. There is still a great tendency to base conclusions on empirical observations rather than on rigid scientific technique in human epidemiologic studies, in which it is so difficult and so important to provide comparable controls.

The method of administering the vaccine has changed three times in this period. Administration by mouth in the early days of life was first advocated. This apparently is gradually disappearing as a method of election. The next method was administration by subcutaneous injection. This was so frequently followed by "cold abscesses" that this also is gradually giving place to the method of intracutaneous injection. Experiments in animals have shown little value for the oral method as a means of prevention. The subcutaneous method and the intracutaneous method are variable in their results in animals. The intravenous method<sup>3</sup> of vaccination has proved to be the most efficacious in cattle, although this also varies within wide limits. The greatest difficulty has been to determine how long the period of increased resistance lasts. This also apparently varies in many instances and is often of short duration; that is, under one year.

Many different cultures of BCG have been

1. GRIFFITH, A. S.: *The Lancet*, 1932, 1: 303, 361.

2. GREENWOOD, MAJOR: *Brit. M. J.*, 1928, 1: 793.

3. BUXTON, J. B. AND GRIFFITH, A. S.: *The Lancet*, 1931, 1: 393.

sent to the United States in the hands of various persons, laymen and physicians alike. Different workers have used cultures obtained at different times from the French laboratories. The result is variation in the experimental work that has been carried on, for little has been done to check the constancy of the characteristics of these strains. When the matter of human use first required attention in the United States, Dr. G. W. McCoy, director of the National Institute of Health, conferred with Dr. Theobald Smith, Dr. William H. Park, Dr. Eugene L. Opie and Dr. William Charles White. It was agreed that Dr. Park and Dr. Opie should undertake to use the vaccine (with the consent of parents) in children in the United States with as careful control conditions as possible. These studies were undertaken with the approval of Dr. McCoy. One study<sup>4</sup> was carried on from the Department of Health of New York City and the other<sup>5</sup> from the Henry Phipps Institute in Philadelphia. The results of these studies have been published from time to time. They are among the best attempts in the world at adequate control comparisons, but one can only conclude, after studying them, that they do not provide conclusive evidence for general use of the vaccine.

It is not the purpose here to analyze the experiments by various persons in different countries but rather to offer certain conclusions based on a careful study of the data and a familiarity with several of the experiments in different countries. The whole subject has been fairly reviewed by K. Neville Irvine.<sup>6</sup> It may be concluded that:

1. Practically all strains of BCG used in children have been avirulent. (Nothing has been said of the Lübeck disaster, as this was proved to be a laboratory accident.)

2. It has been proved that there is a definite increase in the resistance of cattle by the use of this vaccine, although it varies within wide limits and the duration of the increased resistance also varies within wide limits.

3. The evidence of increased resistance produced by this vaccine in many other species of animals is not very convincing.

4. The oral method, if one is to judge by animal experiments, is not efficient.

5. One is not justified in taking the animal experiments, even those in cattle, as a reason for universal vaccination in man.

Sufficient arguments can however be presented for the use of this vaccine in groups for which

4. KERESZTURI, CAMILLE, PARK, W. H., VOGEL, P. AND LEVINE, M.: Fate of children of tuberculous families, including those treated and those not treated with BCG, *Am. J. Dis. Child.*, 1934, **48**: 507.
5. ARONSON, J. D. AND DANNENBERG, A. M.: Effect of vaccination with BCG on tuberculosis in infancy and in childhood, *Am. J. Dis. Child.*, 1935, **50**: 1117.
6. IRVINE, K. N.: The BCG Vaccine, Oxford University Press, London, Humphrey Milford, 1934.

little can be done by other methods, as for example the Negroes in the South and the Indians on the reservations, where the present machinery is not adequate in view of the peculiar circumstances surrounding their condition. It would be possible, under conditions in which a high death rate prevails, over a period of twenty years, to determine something of the value of BCG and also to add to our knowledge. That there is no conclusive proof of the efficacy of the vaccine in man is in part due to the short duration of the experiments and to the small number of those involved in the carefully controlled experiments as well as to the inadequacy of the accurate data on the control groups.—Editorial, *J. Am. M. Ass.*, 1936, **107**: 132.

### Studies in Colds and Influenza

Several bands of patient and privileged workers continue to wrestle with the problem of virus diseases of the respiratory tract. That such work emanates principally from two centres only is due to the fact that unlimited time and expensive facilities are needed for its successful prosecution. Interest has lately been centred on the achievement in this country of propagating the virus of influenza in ferrets and in mice. It need hardly be pointed out that the ability to produce a disease at will in an experimental animal, and to maintain individual strains of the causative micro-organism in this way, is an important step forward and opens the door to new methods of study. One of these is the demonstration of antibodies in human serum by means of protection tests in animals, and experiments on these lines now reported from the United States yield some interesting and puzzling results. Francis and Magill<sup>1</sup> have found that neutralizing antibodies for the virus of influenza are demonstrable in a large proportion of human sera; the puzzling feature of their results is that although the age period 30 to 39 furnishes the biggest percentage of sera containing antibody, the period in which this antibody is most often present in sufficient amount to give complete protection is from 1 to 5 years. Studies by Francis and Shope<sup>2</sup> suggest that there is some antigenic relation, by no means amounting to identity, between the viruses of human and swine influenza, and Shope<sup>3</sup> in another paper, which describes the results of protection tests with human sera and the virus of swine influenza, suggests not for the first time that this virus is the "surviving prototype" of that responsible for the human pandemic of 1918. Meanwhile Dochez and his colleagues,<sup>4</sup> in transmitting influenza virus to human volunteers, have produced more often

1. *J. Exper. Med.*, 1936, **63**: 655.

2. *Ibid.*, 1936, **63**: 645.

3. *Ibid.*, 1936, **63**: 669.

4. *Ibid.*, 1936, **63**: 559, 581.

than not simply a common cold, a result which they are not prepared at present to explain. They have also maintained strains of common-cold virus in culture in a chick-embryo medium through eighty and more generations, and have reproduced the disease in volunteers by intra-nasal installation of these cultures. Dochez has found that the preservation *in vitro* of the cold virus is favoured by the addition of gum acacia. This paper records over one hundred such inoculations of human beings, and mentions that the victims were accommodated in private wards and nursed under the most stringent conditions (stopping short, however, of the actual sterilization of their food) to prevent extraneous infection; but we are not told who they were and by what means or at what expense they were induced to undergo this treatment. Obviously the resources necessary for experiments of this kind are a bar to their execution by all but a few investigators. In one direction only do these observations appear to bear directly on the ultimate aim of all this work—a method of prophylaxis. Necessary and illuminating as all these studies are, there is still one fact which seems to stand immovably in the way of their practical fruition, and that is the evanescence of the immunity conferred by the natural infection. Artificial immunization can scarcely hope to improve on this, and it is therefore difficult to see how such a method could be applied without a degree of trouble disproportionate to the value of its results.—*Brit. M. J.*, 1936, 2: 29.

#### Coramine as an Antidote to the Barbiturates

The great efficacy of coramine as a stimulant to respiration has been recognized for some years. It was recently discussed at a meeting of the section of therapeutics and pharmacology of the Royal Society of Medicine, where, though a little doubt was thrown on its value, the majority expressed their faith in the drug, and some described excellent results obtained from its use in all conditions associated with shock and depressed circulatory and respiratory states. Anæsthetists have often used injections of the drug to improve the breathing when it has shown signs of failing or has actually stopped. This action of coramine has been taken advantage of especially in connection with depression of respiration arising after the use of basal narcotics. An interesting series of clinical experiments is described by Dr. P. G. Schube, which shows the remarkable power possessed by coramine of counteracting the effects of barbiturates. It is not merely the increased depth and frequency of respiration and improved circulation which follow the administration of coramine, but also the extraordinary cutting-short of the unconsciousness that had been induced by large amounts of barbiturate. The

opportunity to test these results arose in the psychiatric clinic of the Boston State Hospital, the patients being all "mentally ill but physically normal". Tests were carried out on 84 patients, the controls receiving barbiturate but no coramine. In the other patients the coramine was given intravenously 5 c.cm. first, and if consciousness had not returned at the end of ten minutes another 5 c.cm. every ten minutes until the patient was conscious. It is stated that in each instance when coramine was injected "the state of unconsciousness was abolished, some persons having to receive more coramine than others to achieve this result". In the controls, unconsciousness lasted for hours longer than in those that had had coramine, in whom it was only a matter of minutes. It is notable that in all these patients the pulse-rate and volume were unaltered although respirations were increased both in rate and in depth. Some of the patients vomited after 10 c.cm. of coramine had been injected. There were no after-effects, and the author concludes that "coramine is an excellent drug to counteract effects produced by barbiturates".—From *The Lancet*, 1936, 1: 1420.

## Medico-Legal

### XXIII.

#### The Evidence of a Bullet Wound

Medico-legal evidence may be of overwhelming importance in proving or disproving guilt. But such evidence often calls for very careful observation. Both these points are well brought out in a case reported by Osborn (*The Lancet*, 1936, 230: 1295). The main point to be decided was whether the victim had been shot from behind or from in front. The accused admitted the shooting, but said that he had fired in self-defence, facing his man; to which the prosecution replied that the nature of the wound showed that it must have been inflicted from behind, making the presumption of wilful murder very strong.

The wound was in two parts; a large and ragged opening at the external angle of the right eye, and a small, clean hole behind this, immediately above the right ear. The brain substance on the right side was extensively macerated, and contained fragments of bone and two pellets of lead. From these findings the Crown examiner concluded that the small clean hole posteriorly was the entry wound, and the large ragged hole anteriorly the exit, from which it followed that the bullet must have been fired from behind. This decision was based on the

widespread belief that bullets make a small wound on entry and a large one on exit, but the defence pointed out that the nature of bullet wounds depends on (a) the kind of bullet, (b) the muzzle velocity of the weapon, and (c) the range at which the shot is fired. In this case, the bullet was of lead with no hard jacket. Such bullets act as dum-dums, immediately mushrooming out on striking the body, and so causing extensive tissue damage at the point of entrance, probably more than at the exit. Again, even if the bullet is hard, (*i.e.*, nickel-jacketed) it is more apt to "wobble" when the muzzle velocity is not very high, and thus to lacerate the tissues at the point of entry. And, finally, at short range, any bullet is apt to cause a large entry wound, as its impact on the tissues is so terrific (virtually an explosion).

To account for the small clean hole, it was shown that the soft lead bullet had broken into three small pieces in smashing through the cranium bone, and that one of these pieces had followed the lateral wall of the skull till it reached the curve-in of the posterior region of the ear. Here it went through and dropped to the floor, where it was found later on.

Another point brought out was the absence of powder-marking around either wound. As the powder used was black and the distance from which the shot was fired very short, only about four feet, there must have been some powder deposited on the tissues at the point of entry, but there was no marking around the small posterior wound. On the other hand, the anterior wound was so extensive that the area of scalp receiving the powder mark had been blown away. There were other arguments, less striking perhaps, but all tending to prove the same thing, *i.e.*, that the bullet must have been fired from in front of the victim, and, accordingly, a verdict of not guilty was finally brought in. Later on, additional suggestions were made by Sir Sydney Smith which brought out even more facts for consideration. He said that if the margin of the wounds in the bone had been examined closely, extremely important evidence could have been gathered by noting the angle of bevelling caused by the bullet. Almost invariably the bone bevels in the direction of fire, so that in this case the posterior wound would have shown at once whether the missile entered or left the skull at that point. Secondly, it was suggested that the fragments of bone found in the brain tissue might have been examined to see if they corresponded with the loss of bone at the posterior opening. If their total area was greater than the loss of bone at this opening, then they must have been driven in by the bullet entering at the anterior wound, for obviously if this were the exit wound, all bone fragments would have been blown outside the skull.

H.E.M.

## Abstracts from Current Literature Medicine

**Artificial Pneumothorax in Lobar Pneumonia.**  
Blake, F. G., Howard, M. E. and Hull, W. S.,  
*Medicine*, 1936, 15: 1.

This article begins with a useful historical summary and analysis of the subject up to date, and also of the various theories advanced as to the influence of artificial pneumothorax on the course of lobar pneumonia. The authors then give their observations and conclusions based on a study of 42 cases in the New Haven Hospital, New Haven, Conn. As a result of certain preliminary experiments they think that the view that lobar pneumonia is a bronchogenic infection, the inception of which is not dependent upon the occlusion of a bronchus by an infected mucous plug, is the most acceptable. Their subsequent observations support the theory that artificial pneumothorax in this disease exerts its influence by limiting or abolishing the constant expansive and contractile motion of the involved lung during respiration and not by accelerating the production of antibodies or by expelling bronchial exudate and draining the lung of inflammatory products. The "lung rest theory" of therapeusis by artificial pneumothorax is to them the most reasonable, even though no evidence has been developed as yet to show in what manner collapse and immobilization of the pneumonic lung, apart from relieving pleural pain, exert a beneficial influence. The induction of artificial pneumothorax is, they conclude, an emergency procedure, and should be carried out without delay early in the course of the disease if a really beneficial effect on the course and outcome of lobar pneumonia is to be obtained. The longer the procedure is delayed, the less likely are the results to be satisfactory. No statistical analysis of their results is warranted, but they think the procedure is worthy of further trial.

A. G. NICHOLLS

**The Psychology of the Tuberculous.** Learoyd,  
C. G., *Brit. J. Tuber.*, 1936, 30: 111.

The author of this arresting paper asks "Is there an attitude of mind characteristic of the tuberculous? Does the toxin produce anything comparable to the relentless depression of influenza, the abject apathy of ankylostomiasis, or the cunning mendacity of opium? It is absurd to suppose that a disease that can modify the rest of the body, so as to give rise, for instance, to the 'tuberculous facies', would not at the same time modify the mental processes. Young patients, especially those with glandular and bone tuberculosis, tend to have mental characteristics of their own; they are gentle and kindly, enthusiastic and excitable, imaginative and amenable, and as a rule content. In the case of

pulmonary tuberculosis, when the action of the toxin is intermittent, the mental state varies, corresponding with the periodic activity of the disease. Anyone who has had a temperature from tuberculosis will recognize that "Treasure Island" faithfully reproduces the tempo of his thoughts. Fishberg has given a long list of authors and poets in whom the toxin of tuberculosis, we may suppose, has supplied some at least of the stimulus to their creative mental processes. Probably the best thing for a tuberculous writer is to be a "leaker", that is, one in whom small quantities of toxin are liberated from time to time, but never in sufficient amounts to do harm. Learoyd thinks that one characteristic of the tuberculous at all times is that their normal attributes, especially, perhaps, their expansive ones, are accentuated—the adventurous becomes more adventurous, the cheery more cheery, and the generous more generous. One very marked type of mentality is not nearly so common in these days of controlled temperature as it used to be—the fervid, fiery, febrile type, the extrovert with a mission and the tuberculous toxin as a driving force within him—a type that is also met with in the alcoholic. There are some who regard a certain cantankerousness, a desire to hurt, a "waspishness", as part of the abnormal mental state of the tuberculous subject. Surely, this is but a normal reaction to adverse circumstances. The young man with his career shattered, the brand of Naaman imagined, cribbed, cabined and confined, or the married man with the clouds of financial embarrassment threatening him, is merely reacting normally to hard conditions. Who would not be the same under similar provocation?

A. G. NICHOLLS

### Surgery

**Relation of Pathological Changes of the Intervertebral Discs to Pain in the Lower Part of the Back.** Sashin, D., *Arch. Surg.*, 1936, 32: 932.

In this article, Sashin draws attention to the importance of pathological changes of the intervertebral discs, particularly those of the lower portion of the spine and of the lumbosacral junction, in the causation of pain in the lower part of the back.

The discs form one-quarter of the total length of the spine. They vary in size, being widest and thickest in the lumbar region and smallest in the dorsal region. In the lumbar region they form a third of its length. They have no blood vessels, but receive nourishment from the bone marrow of the bodies by diffusion. These discs permit a considerable range of motion and impart great flexibility to the spine. They act as a buffer or shock absorber for the strain and stress of daily activity. Mobility of the spine is

greatest in the cervical and lumbar regions and least in the dorsal. Flexion is freest and most extensive in the lower lumbar portion of the spine. Pathological changes in the intervertebral discs are mainly seen after the third decade of life and increase in frequency with age. The changes vary from a small herniation from the disc into the vertebral bodies, to beginning vascular infiltration of the substance of the disc, fibrous replacement of nuclear tissue, brown degeneration, calcification of the nucleus and in later stages, shrinkage, narrowing, and ossification of the disc. The flexibility and mobility of the spine are considerably diminished when degenerative changes are present. Herniation from the discs into the adjacent bodies is frequently found post mortem. These invasions are usually of small size, but, often may extend for a considerable distance into the substantia spongiosa. The great majority of herniations are not visualized by x-rays. Marked degenerative changes of the substances of the disc are often seen, without any evidence of herniation. These changes result from the wear and tear of daily activity. The clinical picture of pathological discs is not clearly demonstrable. The main symptoms complained of are dull aching pains in the lower part of the back, pain radiating down the backs of the lower limbs along the course of the sciatic nerve. There is frequently the history of a slight injury, a slight fall or a sudden twist on lifting an object. The lower lumbar portion of the spine is held rigid; motion of the spine is restricted. There is tenderness over the lumbosacral junction as well as over the area supplied by the superior gluteal nerve. The author's treatment consisted in an attempt to re-establish the normal lumbar lordosis and to support the spine by means of a plaster of Paris jacket. He obtained the best results by gently hyperextending the spine while the patient was under general anaesthesia, until the normal lumbar lordosis was reached, then applying a plaster of Paris jacket from the upper part of the chest to the pelvis.

G. E. LEARMONT

### Obstetrics and Gynæcology

**Regional Anæsthesia in the Conduct of Labour.** Walker, A. T., *Am. J. Obst. & Gyn.*, 1936, 32: 60.

Local block and infiltration anaesthesia have a wide application in obstetrics in the conduct of labour. Most labours can be conducted and successfully terminated with a minimum of pain, low morbidity and mortality by the use of the type of anaesthesia and analgesia described. Many patients so handled do not remember the labour or the delivery.

Abnormal presentations and labours can be successfully conducted with this type of anaesthesia. Episiotomy and repair can be accom-

plished with the same anaesthesia as used for the delivery. Although no definite statistics are available at present, the blood loss during and after the third stage appears to be much reduced with regional anaesthesia.

In addition to producing a relatively painless labour and delivery regional anaesthesia demands careful handling of instruments and respect for tissues which ultimately reduce morbidity and mortality in both mother and infant, and, therefore, constitutes one of the major advantages of this method.

ROSS MITCHELL

**A Study of Three Hundred and Eight Cases of Placenta Prævia.** Irving, F. C., *Am. J. Obst. & Gyn.*, 1936, 32: 36.

A study of 308 consecutive cases of placenta prævia at the Boston Lying-In Hospital shows a decrease in maternal mortality from 11.6 per cent to 2 per cent, and a decrease in net fetal mortality from 47 to 20.3 per cent. In clean cases, where the infant is alive, normal, and of an estimated weight over 4 pounds, Cæsarean section offers about an 85 per cent chance of securing a living child, with a risk to the mother not exceeding 5 per cent.

In clean cases, when the infant is dead, deformed, or under 4 pounds in estimated weight, Braxton Hicks version may be performed by the trained obstetrician at no greater risk to the mother than Cæsarean section. In clean cases of marginal placenta prævia, simple rupture of the membranes deserves an extended trial. It is safe for the mother, and apparently less injurious to the child than has been supposed. In infected cases, Cæsarean section followed by hysterectomy is the operation of choice, regardless of the condition of the child.

ROSS MITCHELL

**Pædiatrics**

**Prognosis of Rheumatic Infection in Childhood.** Ash, R., *Am. J. Dis. Child.*, 1936, 52: 28.

This is a study of 445 children coming under observation for rheumatic fever at the Children's Hospital, Philadelphia, during the period 1922 to 1932. Ninety-three per cent of these children were observed for an average period of seven and a half years after the onset of their disease. At the end of this time 66 per cent showed valvular disease of the heart and 22 per cent had died.

The course of the affection was modified by such variables as race, sex, age and the calendar year of the origin.

Among the clinical manifestations which were of the most serious omen were pericarditis, rheumatic pneumonia; involvement of both mitral and aortic valves, the early appearance of a button-hole mitral stenosis, and obtrusively

large subcutaneous nodules. Chorea, in itself, was a mild manifestation. In an intermediate group may be placed epistaxis, abdominal pain, haematuria, and the multiform cutaneous eruptions.

The crucial period for treatment is during the first year after the inception of the disease, inasmuch as when permanent cardiac damage occurs it does so before the end of the second year after the onset.

JOHN NICHOLLS

**Appendicular Symptoms in the Acute Infectious Diseases.** Ronaldson, G. W., *Brit. J. Dis. Child.*, 1936, 33: 85.

The appendix is frequently involved in the acute infectious diseases, though suppurative appendicitis is rare. Appendicitis is mentioned as a complication of scarlet fever, measles, small-pox, rubella, typhoid and malaria. Some French authors attach considerable importance to its supposed relationship to scarlet fever.

Ronaldson finds that in London appendicitis severe enough to call for operation in cases of infectious disease is quite rare. In one London infectious hospital, in 20,000 cases, there were only 2 operations for appendectomy; in another there was only 1 appendectomy (in scarlet fever) in a series of 7,659 fever cases. He reports two cases of his own of operation for acute appendicitis, one with abscess and one with gangrene, in scarlet fever, at the South-eastern Hospital. These cases are illustrations of the well-recognized fact that abdominal conditions in young subjects may pursue an insidious course and so occasion difficulty in diagnosis. In his cases the association of appendicitis with scarlet fever may have been quite fortuitous. He states, further, that though suppurative appendicitis is very rare in measles pain localized to the iliac region may be an early feature in that disease. These are the cases of what Mayerhofer calls "pseudo-appendicitis". It is important to remember that this symptom may occasionally be present. When the eruption of measles occurs, on the fourth day, the tendency is for the acute iliac pain to subside. The discovery of Koplik's spots will establish the diagnosis and prevent too hasty surgical interference.

JOHN NICHOLLS

**Morquio's Disease. Report of Two Cases.**

Summerfeldt, P. and Brown, A., *Arch. Dis. Childhood*, 1936, 11: 221.

This rare condition, of which only 18 cases have been reported in the literature according to the authors, is characterized by dwarfism, deformity of the body due to changes occurring chiefly in the vertebræ, pelvis and long bones caused by delayed epiphyseal development and retarded ossification. Only 3 of the 18 have been isolated cases; the remaining 15 have occurred

in children where other members of the family were affected. The family reported by the authors consisted of two normal girls, two normal boys, and two affected boys. The parents were not related. The use of pituitary and thyroid extract and of viosterol by other authors proved of no benefit. The younger of the children in this family was put on cod liver oil and calcium tablets, the latter only being taken. The mother reported that he had gained in height, an observation not yet confirmed by examination by the physician. The older boy was given thyroid. No statement as to the result was given.

MADGE THURLOW MACKLIN

### Pathology and Experimental Medicine

**The Moppet Test for Cancer.** Welsh, D. A., *J. Cancer Res. Com. Univ. of Sydney*, 1936, 7: 132.

Professor Welsh gives a review of the Moppet test with valuable comments. Briefly, the test is as follows. The blood to be tested and blood from a healthy control are placed in opposite ends of a special diffusion vessel which is filled with normal saline after the bloods have clotted. A fragment of mouse tumour (sarcoma) is placed on a glass plate, which is then inverted over the diffusion vessel so that the fragment of tumour lies midway between the two clots. An initial reading (drawing) is taken of the periphery of the tumour fragment. The diffusion vessel is then incubated at 37° C. and the readings are taken at one hour and at twenty-four hours. In a negative reaction there is a more or less symmetrical "outwandering" of cells from the fragment of sarcoma; in a positive test for cancer there is a definite "sweeping" movement of the sarcoma cells away from the cancerous patient's blood.

Dr. Moppet has given the results of 23 tests made on unknown bloods in addition to those of the 30 published in an earlier paper. Of the 23 tests 8 gave a positive reaction for cancer, and of these eight 5 were correct and 3 were incorrect. Admittedly, this is a poor showing and indicates the necessity for further improvement in the technique. However, both in its successes and its failures the test has raised questions of great scientific interest and promises to be of practical value.

Dr. E. F. Thomson has, also, made an independent investigation of the test, covering 100 cases, with unexpectedly good results. Thirty-six gave a positive reaction for cancer, 33 of which were in patients clinically cancerous and 3 in patients not clinically cancerous. According to the available evidence, however, these 3 had probably developed cancer at some time. It is noteworthy that the 33 positive reactions were found in patients in the early stages of cancer,

before anaemia and wasting had occurred. Objection might be taken that these 33 correct positive findings for cancer were of little practical value, inasmuch as a biopsy might have been made in all or nearly all of the cases, but this is not the point. The significant fact is that a correct positive cancer reaction was found in 92 per cent of cancers in the early stages from many different anatomical sites. This suggests that the Moppet test has a scientific significance which must be farther explored before its clinical usefulness can be properly assessed.

JOHN NICHOLLS

### Amidopyrine and the Circulating Leucocytes.

Simon, S. D. and Metz, M. H., *J. Lab. & Clin. Med.*, 1936, 21: 1154.

There is little doubt that in certain persons amidopyrine is competent to produce granulocytopenia; there is no doubt in most minds that the vast majority of people can take the drug without developing this condition. This latter statement would seem to be self-evident and yet it rests on no proper basis of investigation. The authors, therefore, have endeavoured to supply the lacking evidence. Their paper is based on the study of 103 patients whose history was followed up for an adequate length of time. Those suffering from severe disease of the heart or the blood-forming organs were excluded from the test. The majority of the persons studied were in the 5th, 6th and 7th decades of life; the remainder were scattered fairly uniformly in the 2nd, 3rd, 4th and 8th. All received amidopyrine, and 20 of them in addition received isoamylethyl barbituric acid (amytal). In not a single instance did a significant decrease in the number of leucocytes occur. In one case an actual leucocytosis was observed (the highest count was 16,000 with 86 per cent neutrophiles), accompanied by nausea and malaise. The total amount of amidopyrine given varied in the different cases from 14 to 49 grams, spread over 14 to 49 days. The sedimentation rate was not affected in any of the 8 cases in which this test was performed. No morphological alterations, such as "toxic granules" in the neutrophiles, were observed. The differential count, also, was not affected in any significant fashion.

The authors conclude that the entirely negative results of their experiment would seem to substantiate the widely-held opinion that granulocytopenia when associated with amidopyrine medication is a matter of individual susceptibility.

JOHN NICHOLLS

### Morphological Changes in the Heart in Experimental Myxœdema.

Webster, B. and Cooke, C., *Arch. Int. Med.*, 1936, 58: 269.

The question is raised as to whether in myxœdema cardiac enlargement and the presence

of low voltage in electrocardiograms are found. The authors have investigated the problem by removing the thyroids from a group of rabbits and examining the hearts after a considerable lapse of time. Their autopsy findings were compared with similar tissues from controls.

There was some variation in the degree, but myxœdema was produced in all cases, corroborated by an increased blood-cholesterol content, loss of hair, and in some cases effusions into the serous cavities. The hearts of all thyroidectomized animals were pale and flabby, with increased fluid content. The muscle stained poorly, the fibres were swollen, with loss of fibres, especially of the transverse type. The nuclei stained deeply and were surrounded by a clear area, not composed of fat. The aortas showed very little change. Some atrophy of testicular and ovarian tissue was noted. Electrocardiograms showed a gradually decreasing voltage, as registered by the height of the T-wave and the Q.R.S. complex.

P. M. MACDONNELL

### Therapeutics

#### The Treatment of Carcinoma of Cervix Uteri by the Stockholm Technique at the London Hospital. Brews, A., *The Lancet*, 1936, 1: 713.

In two years, 1929 and 1930, seventy-one cases of cancer of cervix were treated at the London Hospital. Of these, four selected had Wertheim's hysterectomy done, with the subsequent history that one died of recurrence one year and five months after operation; one died of recurrence two years and eight months after operation; one, last seen one year and nine months after operation, was alive and well; and one is alive and well more than five years after operation. The remaining 67 cases were treated by radium, by the Forssell-Heyman technique from Radiumhemmet, Stockholm, e.g., 120 mg. of radium, three applications at seven and twenty-one day intervals; duration of each application 22 to 24 hours; screenage 2 mm. of lead in 1929 and 3 mm. of lead in 1930; partly intra-uterine and partly vaginal. No case, however advanced, was refused treatment.

The diagnosis was confirmed in all but 8 cases by histological examination.

The results show 16 five-year cures out of 67 treated by radium, or 24 per cent. On grouping the 67 cases into the four stages according to the anatomical extent of the growth, as recommended by the Radiological Sub-Commission of the League of Nations, Geneva, 1929, the first stage showed 40 per cent five-year cures; the second, 30 per cent; the third, 16.6 per cent; the fourth, none. The first and second stages are probably operable, and if the results are combined they show 34.3 per cent five-year cures.

The third and fourth stages are probably unoperable and combined show 12.5 per cent five-year cures. At Radiumhemmet, Stockholm, in ten years, from 1920 to 1929, they treated 1,295 cases of carcinoma of the cervix, with 23.8 per cent five-year cures.

S. A. McFETRIDGE

#### The Effect of Oophorectomy and Splenectomy on Cancer of the Breast and Uterus. Paterson, P., *The Lancet*, 1936, 1: 1402.

The unlimited multiplication of the cells in cancer is generally explained by two factors—first, the abnormal stimulation of the cells primarily involved; and second, the medium in which these can grow. The author considers the latter the more important. He offers no opinion as to the cause of this change which takes place in the tissues. He gives examples of tumours which were proved to be malignant and have disappeared spontaneously. The first case was a young woman who, one year following appendectomy, developed a mass in the right iliac fossa. At operation, the mass involved the cæcum. Microscopically, it was shown to be a spindle-celled sarcoma. Following operation, a large abscess developed (*B. coli*), and when this cleared up the mass gradually disappeared and today she is alive and well.

The second case was carcinoma of the stomach, with secondaries in the liver. This was confirmed by microscopic examination. Nothing further surgical was done, except to close the abdomen, and the patient is alive and apparently well today.

The high immunity of the spleen to primary and secondary cancer suggested trying to use an extract to control cancer. As a result of these injections, Paterson came to the conclusion that the growth was stimulated by these injections, and the larger the dose, the more rapidly did it advance. Consequently, he tried removal of the spleen.

The third case was a woman of 41 years of age, who two years previously had had both ovaries and uterus removed for adeno-carcinoma of the uterus. She now had a secondary tumour in her pelvis, involving the rectum (blood pus and mucus) and bladder (urine containing pus and blood). She required narcotics for pain and sleep. A left inguinal colostomy and splenectomy were done, followed by 4 c.cm. daily of splenic extract for six weeks. Her condition became progressively worse, but improved when 1 c.cm. was given daily for two months. Now, four years later, there is no evidence of disease.

The fourth case was a woman, 46 years of age, with cancer of the right breast of at least one year's duration. The mass was firmly fixed to the chest wall, there were glands in axilla, skin nodules and widespread lymphatic involvement. Microscopic examination of the glands showed

adenocarcinoma. The spleen and both ovaries were removed. No other treatment was given. Ten months after operation the lymph glands in the axilla were no longer palpable, the cutaneous nodules had all disappeared, and the breast was a shrivelled fibrous mass. The patient gained a stone in weight.

Removal of the ovaries or the spleen does not affect the course of the cancer, and these cases were just presented as a possible help or guide to other workers in this field.

S. A. McFETRIDGE

**The Treatment of Surgical Infections with the New Chlorine Solutions.** Young F., *Surg., Gyn. & Obst.*, 1936, 63: 318.

The author reports on the use of a new chlorine compound, N-N'-dichloroazodicarbonamide (azochloramide), in contaminated and infected wounds. Azochloramide has been the subject of a few papers during 1935 and 1936. It possesses bactericidal properties of a high degree, but it is peculiarly inert against organic matter. It is the least irritating chlorine compound so far produced for surgical purposes. Azochloramide was used as an oily solution of triacetin 1:500 in all cases except for irrigation in empyema, when saline concentrations of 1:1,666 and 1:3,300 were believed to favour more ready absorption from the pleural cavity. There is evidence to indicate the triacetin solution is removed rather promptly, however. Young does not mention any deduced values from the use of the two saline concentrations. The value of azochloramide was judged by comparing a similar number of cases treated before this new chlorine compound was available, termed respectively control and experimental cases.

Identical incisions were made in operations for hydronephrosis, pyonephrosis and nephrolithiasis. Ten control and 7 experimental cases are compared. All cases were drained. The control cases with pre-operative positive urine cultures were irrigated with saline, Dakin's or mercurochrome solutions when infection became evident. The experimental cases with pre-operative positive urine cultures were treated by filling the drainage tube with azochloramide, beginning 24 hours after operation. Of the 10 controls 7 had positive urine cultures of *Staph. aureus* (4), *B. coli* (2), and *Staph. albus* (1). They healed in an average of 52 days. Of the 7 experimentals all had positive urine cultures of *Staph. aureus* (2), *B. coli* (3), non-haemolytic streptococcus (1), and *B. proteus* (1). Five of the 7 experimentals remained sterile and healed in an average of 15 days; 2 had perinephric abscesses in which the healing time averaged 30 days. Apparently, the azochloramide solution is capable of preventing infection in contaminated wounds.

In empyema, 7 controls and 6 experimentals were compared. The routine was aspiration until optimum time for surgical drainage. On the second day after drainage the cavity was filled with Dakin's or either of the two azochloramide saline solutions every four hours. The drainage tube was closed off for one hour, and then suction was applied. The 7 control cases were infected with *Pneumococcus I* (3); *Pneumococcus IV* (3), and *S. haemolyticus* (1). The cavities were treated as follows; closed drainage (3); rib-resection after closed drainage (3); primary rib-resection (1). They healed in an average of 83 days. The 6 experimental cases were infected with *Pneumococcus I* (1); *Pneumococcus II* (1); *S. haemolyticus* (2); anaerobic streptococcus (1), and *Myco. tuberculosis*, *Staph. aureus* and *B. pyocyanus* (1). The cavities were treated as follows; closed drainage 2; primary rib-resection 3; and the one with triple infection finally by thoracoplasty. Two were irrigated with the 1:1,666 and 3 with the 1:3,300 solution. These 5 healed in an average of 41 days. The discharge from the experimentals was relatively much thinner in quality. It was possible to control the *Staph. aureus* with azochloramide solution and the *B. pyocyanus* with 0.5 per cent acetic acid, but either one of the organisms was constantly present, with the tubercle bacillus.

In infection with coincident diabetes, it is more difficult to draw conclusions because of the distinctly individual nature of each case. Eight controls healed in 87 days; 9 experimentals treated with packing every 24 hours healed in 64 days, both after amputations of one toe. In 5 controls with diabetes and carbuncles of an average diameter of 6 cm. treated with Dakin's solution the average healing time was 45 days; in 5 experimentals, with the same locations, of an average diameter of 8 cm. treated with daily packings the average healing time was 29 days.

The author also cites other cases of debridement in traumatic injuries packed with azochloramide in 1:500 triacetin, and the satisfactory results obtained in infected post-operative abdominal wounds with like results, and of bone infections, in which, however, the results were not so happy. Young allows full value to Dakin's solution in removal of necrotic tissue.

FRANK DORRANCE

**Use of Urea to Stimulate Healing in Chronic Purulent Wounds.** Robinson, W., *Am. J. Surg.*, 1936, 33: 192.

The author's interest was aroused after having used allantoin for a similar purpose. Allantoin is claimed to be one of the beneficial agents in the surgical use of maggots. The beneficial action of urea depends upon the stimulation of indolent tissues to produce granulation tissue

and a more abundant blood supply. Urea readily permeates the membrane of all cells. He cites a number of case reports to show rapid healing in such lesions as osteomyelitis of the femur, gangrene after frost-bite, cellulitis, abscesses of limbs and trunk, infected burns and varicose ulcers. The author states that urea is active only during the time it is in contact with the affected part, and that healing is evident by 72 hours after the commencement of treatment. A 2 per cent solution in sterile, cold distilled water has been found to be of most practical value, although a 10 per cent solution has been used in resistant cases. He has used it as a "hot soak" for one-half hour three or four times a day; as thoroughly saturated moist compresses loosely applied and covered with oiled silk or waxed paper; by syringing into sinuses or inaccessible parts and changing the dressing as indicated; as a bath of 0.25 per cent; and as a 15 per cent ointment in vanishing cream or other greaseless ointment base.

FRANK DORRANCE

### Anæsthesia

**The Meaning of the Phrase "A Good Anæsthesia".** Charles, R. L., *Anæsthesia & Analgesia*, 1936, 15: 206.

The author defines the phrase in his presidential address at the Southern Medical Association Week in St. Louis, Miss. In so doing he realizes fully the three individuals directly affected, the patient, the surgeon and the anæsthetist. Some patients wish to go to sleep quickly or to leave their room in an unconscious state, others wish to avoid nausea, and mostly everyone wishes to be assured of awakening with the promise of better health in the future. The surgeon wishes to perform freely and fully his work without having to give thought to the patient's condition and to be assured of as little after-effect as possible; sometimes he does not realize these two states are not compatible. The anæsthetist wishes to avoid undue apprehension on the part of the patient. The author likes to make an appraisal of the risk the evening preceding operation. He believes it to be his duty to go over the case-record and to have a professional visit at the bedside. Fear allayed prevents depletion of the alkali reserve and lessens the likelihood of shock. The pre-operative sedative dose can be estimated at this visit or early in the morning. The author dislikes routine orders. He gives his anæsthesia according to the "Law of Anæsthetic Accommodation". The concentration of the drug administered is more often responsible for tissue injury than the length of the anæsthesia. Statistics are more often the measure of the

physician than of the drug. All anæsthetics are potentially dangerous, and particularly so in the hands of the one who is afraid or is over-confident.

FRANK DORRANCE

### Evipal Anæsthesia: Résumé of 1,000 Cases.

McNelis, P. J., *Anæsthesia & Analgesia*, 1936, 15: 199.

The author gives his experience as a private anæsthetist with evipal in a service where minor surgery of the traumatic type is of routine nature.

In traumatic surgery one usually finds a patient with a full stomach, moderately shocked, and in dread of the loss of his earning ability. These patients like evipal because of its lack of post-operative nausea and vomiting and the feeling of comfort and diminution of pain which follows.

McNelis was able to obtain fully satisfactory anæsthesia in such lesions as debridement of burns, suturing of wounds, drainage of abscesses, dilatation and curettage, radium implantation in the cervix, enucleation of eyes, cystoscopies, bronchoscopies, haemorrhoidectomies, pelvic examinations, skin grafts, facial surgery, amputation of digits, to supplement spinal anæsthesia and all types of dental surgery. Injections of morphine and atropine, 45 minutes to one hour prior to tonsillectomies, reduction of fractures and appendectomies, gave more satisfactory conditions for the necessary procedures. In rib-resection, in minimal doses, repeated, with due respect to inhibited respirations, evipal anæsthesia was ideal. The use of evipal does not do away with the need of an anæsthetist at an operation. It has been found advisable to have a carbon dioxide and oxygen apparatus at hand, as well as coramine and so forth. The dose in children of 4 to 7 years was generally 2 to 3 c.c. He found 5 c.c. to be the maximum dose in children under 12 years of age. In males from 12 to 16 years post-operative restlessness was common until the dose had been increased to practically adult limits; adolescents have a high tolerance for barbiturates. The maximum dose given in this series was 4 injections of 10 c.c. each of the 10 per cent solution.

The author believes that evipal has a distinct place in our list of anæsthetics. It is best suited to the realms of minor surgery of traumatic origin. It should not be allowed to take a place with those accepted drugs whose qualities have earned them their place in the realms of major surgery. He does not believe it will come to act as a "pinch-hitter" in basal anæsthesia, nor to supplement spinal anæsthesia.

FRANK DORRANCE

## Obituaries

**Frederick William Marlow, M.D., C.M. (Trinity), F.R.C.S. (Eng.).** died at Knollview, his farm in Scarboro, on August 22, 1936.

Born in Cartwright, Durham County, May 25, 1877, the son of the late Nelson and Ann (Parr) Marlow, he received his early education in the public school, matriculated from the Port Perry High School, entered Trinity Medical College in 1896 and graduated with honours in 1900. He served as a house surgeon in St. Michael's Hospital for a year and then proceeded to London, where he continued his studies at University College, Middlesex and King's College Hospitals, passed the examinations of the conjoint board for the M.R.C.S. (Eng.), L.R.C.P. (London) in 1902, and a year later the examination for the Fellowship of the Royal College of Surgeons. Returning to Toronto, he was appointed to the staff of St. Michael's Hospital as assistant surgeon in 1903, and the following year became surgical registrar at the Toronto General Hospital, being attached to the service of the late Professor J. F. W. Ross, in the department of gynaecology, from 1904 to 1911. He was demonstrator of anatomy, University of Toronto, from 1903 to 1906, and in 1913 was appointed associate professor of gynaecology, University of Toronto, and senior attending gynaecologist to the Toronto General Hospital. He performed the first surgical operation in the new building on College Street. He was also a member of the surgical staffs of St. John's and the Wellesley Hospitals and one of the founders of the American College of Surgeons in 1913.

Dr. Marlow was keenly interested in military medical affairs, joining the Canadian Army Medical Corps on its organization in 1900, and thereafter served in all ranks from private to Lieutenant-Colonel. During the Great War he was A.D.M.S., Military District No. 2, and Inspecting Officer of the C.A.M.C. throughout Canada.

In 1906 he married Florence Elizabeth Walton, of Thorold, having one daughter, Dorothy, who died in 1916.

Of commanding presence, keen, forceful, an indefatigable worker, a ready speaker, and of pleasing personality, Dr. Marlow early established himself in practice and soon became widely known for his skill and sound judgment in his special sphere of abdominal and pelvic surgery. He was President of the Ontario Medical Association in 1919, and of the Academy of Medicine in 1928, and in both offices he showed fine administrative ability.

Dr. Marlow had been in failing health for the past eleven years, his illness beginning in 1925 with diabetes and arterial hypertension with severe oral, tonsillar and sinus infections, followed a year later by reactivation of a duodenal ulcer from which he had suffered previous attacks. After a game of golf late in April, 1927, he suffered a severe attack of coronary thrombosis, and later still of pleurisy with effusion requiring paracentesis at two or three week intervals for nearly a year. His numerous ills were borne without murmur or complaint. Assisted by his fine physique, he eventually overcame his most urgent symptoms and regained a measure of health that permitted his resuming his professional duties during the past five years. Two years ago he purchased a farm near Toronto, erected fine buildings and he followed his agricultural diversion with his wonted enthusiasm and interest. He was about his usual duties on the farm and after a pleasant day, retired on the evening of August 21st. He rang for the nurse at midnight, but passed away a few minutes after she reached the bedside. His widow, two sisters and a brother survive him.

The impressive and beautiful funeral service in St. Paul's Church, conducted by Bishop Renison and the Reverend Dr. Cody, President of the University of Toronto, was largely attended by professional confrères, patients and personal friends, a striking tribute of their esteem for a distinguished surgeon and a fine citizen.

H. B. ANDERSON

**Dr. Charles Eugène Coté** died on June 26th at his residence in Quebec, aged 69. He had been ill for several years. He was born in Quebec and studied at the Petit Séminaire, taking his medical course at the University of Laval where he graduated in medicine in 1890. His practice was largely in St. Sauveur and he was also interested in politics, being elected to the Legislative Assembly in 1906.

**Dr. Mark Dunning**, of Mono Mills, Ont., died at Guelph on August 22, 1936.

Dr. Dunning was born in Lloydtown, near Schomberg, in York County, and came to Summerset Farm, west of Orangeville, as a youth.

After graduating from the University of Toronto (1891), he practised for a year at Athlone in Simcoe County and then moved to nearby Mono Mills, where he practised 42 years. Recently he moved back to the Summerset Farm.

Surviving are two sisters: Elizabeth Dunning, Summerset Farm, and Mrs. Georgina Shannon.

**Dr. Emile Fortin** died suddenly on May 17th at the Hotel Dieu in Quebec, aged 58. He was born at Pointe-Levis, studied at the College of Levis and the University of Laval, Quebec, whence he graduated in medicine in 1904. Dr. Fortin in addition to his medical work was prominent politically and in 1935 was elected to the Senate.

**Dr. A. R. Griffith**, medical superintendent of Montreal Homeopathic Hospital, died on September 2, 1936, in the hospital which he practically created, in his 72nd year, after two months of failing health.

He was the only surviving medical member of the group which founded the Homeopathic Hospital in 1894. He devoted his life to its interests and it was largely due to his unfailing energy that the new building on Marlowe avenue was erected in 1927.

Dr. Griffith was born in Welland, Ont., and received his early education in Grand Forks, North Dakota. He worked his way through college by reporting for the *Grand Forks Herald* while attending the University of North Dakota, in Grand Forks. Later he completed his medical training at the University of Michigan and the Flower Hospital, New York. He came to Montreal in 1892, and started a medical practice which attained wide proportions.

Following the erection of the new Homeopathic Hospital here, he used all his influence and powers of persuasion to induce the American Institute of Homoeopathy to hold its annual convention in Montreal. The convention came here in 1929, and Dr. Griffith was elected president for the following year.

He is survived by his wife and four sons, Dr. J. J., surgeon of the Homeopathic Hospital; Dr. Harold R., a leading authority on anaesthesia; Arthur, and Hugh B.; a brother Thomas, in Grand Forks; a sister Ada, in California, and seven grandchildren.

**Dr. Alexander Hotson**, of Parkhill, Ont., died on July 21, 1936, at his residence, where he had been ill only a short time. He had practised medicine in Parkhill for over 38 years. He observed his 91st birthday on June 17th last in good health.

Dr. Hotson first attended the East Zorra school and then the Retho school, both in Oxford County. Later, he went to the Baptist Literary Institute at

Woodstock. After completing his course, he taught school for about six years in Oxford County before going to Toronto Normal in 1874. When he completed his year there he went to London as principal of the then St. George's School, and the next year to the old Union School in London.

In 1878, Dr. Hotson joined the teaching staff of the London Collegiate Institute as a science teacher and it was while teaching there, he took his medical course and was the second student to enroll in the medical school at Western University at that time. He received his medical degree in 1889. During his last two years, before he stopped teaching, with the permission of the Board of Education he lectured in biology to the medical students. That year he came to Parkhill and took over Dr. Oven's practice. Dr. Hotson was a member of the Microscopic Society in London, which later brought Dr. A. B. MacCallum from Toronto to London to give them a course in bacteriology. This was the first bacteriology course given in London.

He married Miss Annie Jones, of Ailsa Craig, in 1870. She died in 1896. Dr. Hotson leaves one daughter, Miss Aletha Hotson, of Parkhill, high school teacher; one son, Arthur E., a chemical engineer, of Shreveport, La.; a brother, Dr. John Hotson, Vancouver, and a sister, Mrs. Mary Hill, London.

**Dr. Wray Devere Marr Lloyd** died, as the result of an accident, on June 2, 1936, at Rio de Janeiro, Brazil, where he was prosecuting studies on yellow fever. He was thirty-three years old.

Dr. Lloyd was born at Collingwood, Ont., and was a graduate of the University of Western Ontario (1926). After graduation he spent three or four years at the University of Toronto, doing research work at the Banting Institute, where he was associated with Sir Frederick Banting and Prof. Oskar Klotz. He then went to the Rockefeller Foundation in New York and while there discovered a preventive for yellow fever. Both he and Dr. S. F. Kitchen, another Western graduate, were bitten by monkeys and contracted the disease.

Being immune from yellow fever after once being sick with it, Dr. Lloyd was sent to Africa, and later to South America by the Rockefeller Foundation, to continue his studies of the disease where it is most commonly experienced. Two months before his death, he returned from an eight-month sojourn in the jungle of South America securing samples of blood from the natives for test purposes.

Dr. Lloyd was a brilliant student and exceptionally thorough, and his death is a distinct loss to medical science.

He is survived by his widow, his parents, Mr. and Mrs. C. W. Lloyd, of Toronto, and a sister, Marie.

**Dr. James Edward Lovering**, of Lethbridge, Alta., died on August 11, 1936. James Edward Lovering was born at Coldwater, Ont., on November 5, 1871, the son of the late John Lovering and Mary Lynch. He became a school teacher as a young man and taught for nearly 12 years in the interior of British Columbia, spending considerable time at Revelstoke. Returning east he graduated with a medical degree from McGill University in 1908 and in the same year came to Magrath where he practised medicine for three months. He moved to Lethbridge in the fall of 1908, practising his profession continuously until June of this year when he retired.

At the time of his death Dr. Lovering was chairman of the Lethbridge public school board. Education had long been one of his chief interests and he had served on the local board for many years. He

was also active in southern Alberta and provincial educational circles.

Dr. Lovering acted as surgeon to the Royal Canadian Mounted Police in Lethbridge continuously from 1921 until June of this year when his health failed. He was named a coroner for his district many years ago.

Dr. Lovering was married in Lethbridge to Bessie Cronkhite soon after coming to the city. One daughter, Mrs. Bessie Marie Samson, of Lethbridge, was born to this union. Mrs. Lovering passed away in 1911, and in 1913 Dr. Lovering married Sadie M. Greenaway, who survives.

**Dr. Amedée Marien**, of Montreal, surgeon-in-chief of the Hôtel-Dieu, and a former professor in the University of Montreal, died on September 1, 1936, at the age of seventy-one.

Dr. Marien was born in the village of Rivière des Prairies on the Back River. He studied first at l'Assomption College. After graduating there he studied medicine at the Ecole de Médecine Victoria, which later became the faculty of medicine of Laval University, eventually becoming linked with the University of Montreal. He then went to France and studied for some years at the Institut Pasteur. He introduced here on his return many methods then practised in European hospitals. While in France he studied under such prominent French medical leaders as Wineberg, Brault and Legueux, at a time when France was leading the world in medical progress after Pasteur's discoveries. He was one of the first members of Montreal's old Société de Médecine, which later became the Union Médicale du Canada and was one of the founders of the Association of French Speaking Doctors of North America.

**Dr. Arthur Dalton Smith**, of Mitchell, Ont., died on August 30, 1936. He was born in 1858 and a graduate of the Medical Faculty, Trinity University (1882).

**Lieut.-Col. A. M. Warner**. It is with deep regret that we note the death on July 18th of Lieut.-Col. A. M. Warner, B.A., M.D., C.M., Vancouver, after an illness of nine months. Born at De Lewisville, Ontario, Dr. Warner was educated at Cayuga, and graduated from Queen's University, taking his degree in Arts in 1910 and in Medicine in 1912. He became an intern at the Vancouver General Hospital and entered private practice in Vancouver in 1913. He was a valued member of the Vancouver Medical Association and the British Columbia Medical Association.

In 1916 Dr. Warner went overseas with the R.A.M.C. and was appointed O.C. of the Carrier Depot Hospital at Dar-es-Salaam, in German East Africa, which he had built and organized. During his command there 13,000 patients were admitted. He was then sent to Lindi to organize a hospital on similar lines, but became dangerously ill with malaria and was invalided to England. Because of recurrent attacks of malaria he was unfit for service abroad and was attached to Balloon Squadron, Outer Defences of London, as M.O. for a year.

On his return to Canada he rejoined the C.A.M.C. and became attached to the 18th Field Ambulance. He was Officer Commanding the Field Ambulance from 1926-1930, and was appointed Deputy District Medical Officer of Military District No. 11 for four years. He was also O.C. of the Casualty Clearing Station.

Lieut.-Col. Warner was mentioned in despatches by General Van de Venter, and qualified for the Long Service Medal in the C.A.M.C.

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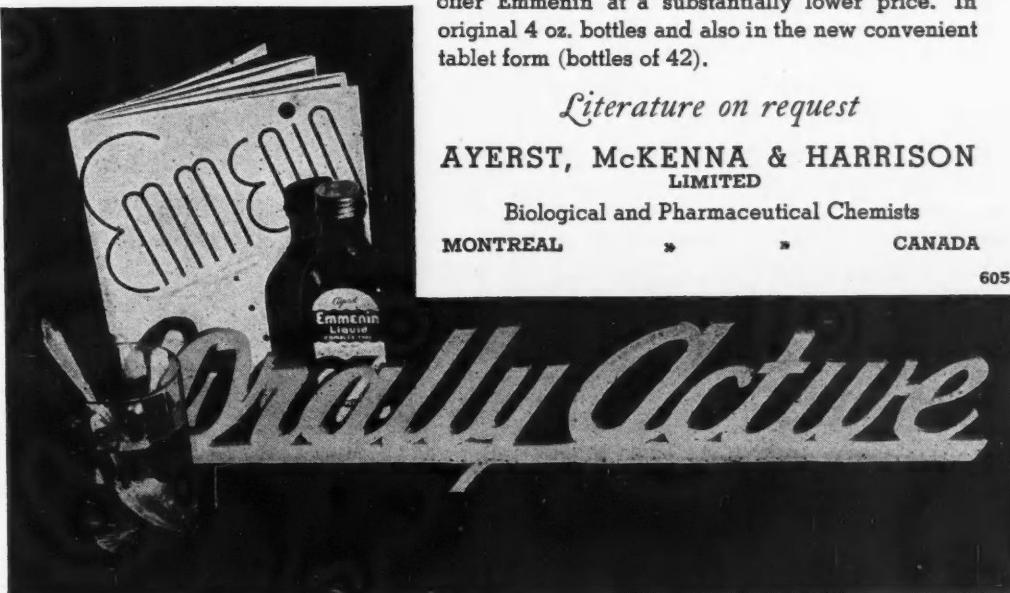
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## News Items

### Great Britain

**The Bureau of Human Heredity.**—The object of this Bureau is collection on as wide a scale as possible of material dealing with human genetics. Later, the tasks of analysis of material and distribution of the information available will be added.

The Bureau is directed by a Council representing medical and scientific bodies in Great Britain. It is affiliated to the International Human Heredity Committee, which ensures cooperation in all areas where research is proceeding.

The Council would be grateful to receive all available material from institutions and individuals, furnishing well-authenticated data on the transmission of human traits whatever these may be. Pedigrees are particularly desired; twin studies and statistical researches are also relevant. As research workers and others who send in material may in some cases wish to retain the sole right of publication (or copyright) those who so desire are asked to accompany their material with a statement to that effect.

Material should be given with all available details in regard to source, diagnostic symptoms and the name and address of the person or persons who vouch for accuracy. All such details will be regarded as strictly confidential.

Reprints of published work would be most acceptable. Further, many authors when publishing material may also have collected a number of pedigrees which they have been unable to reproduce in detail. It is the object of the Council that such records, by being included in the Clearing House, should not be lost.

Those wishing for a copy of the Standard International Pedigree Symbols may obtain one from the office.

Announcements in regard to the services undertaken by the Bureau will be published from time to time.

*Chairman:* R. Ruggles Gates. *Executive Committee:* R. A. Fisher, J. B. S. Haldane, E. A. Cockayne, J. A. Fraser Roberts, L. E. Halsey (Hon. Treasurer), C. B. S. Hodson (Hon. Gen. Secretary). (115, Gower Street, London, W.C.1, England.)

### Alberta

The Alberta Government has indicated that they will pay basic dividends to all eligible covenanters in a few weeks, the amounts and dates are still unfixed. It has been hinted that medical men will be asked to accept a portion if not all their fees for the care of those on relief in credits. If these credits have 100 per cent purchasing power for Alberta products the results may not be so serious.

G. E. LEARMONT

### British Columbia

Work is being started on the new wing of the Kings' Daughters Hospital at Duncan, which will increase the building's capacity from 60 to 85 beds. The two-storey addition will contain men's medical and surgical wards on the ground floor, an Indian section with wards for men, women and children, and a modern diet-kitchen. The second floor will be occupied by private and semi-private rooms, a children's ward and nurses' dining-room.

Dr. S. C. Peterson, formerly of Winnipeg, has been appointed by the Provincial Government as director of venereal disease control for British Columbia. A reorganization of this department of the Provincial Health Department is contemplated, and the government

has increased its appropriation for venereal disease control from \$30,000 to \$45,000.

Dime-in-the-slot "blood-pressure machines," such as have been operating in amusement-parks and on street-corners in various cities of the United States, and which have been banned—if we are not misinformed—in some places, have made their appearance on Vancouver streets. Much interest has been shown by the lay-public and patronage of this new "amusement device" has been generous. To protect himself from the charge of practising medicine without a license the concessionaire has set up signs reading, "Attendant is forbidden to diagnose, prescribe or treat under any circumstances. The only purpose of this machine is to let you read your blood pressure and nothing else." The medical officer of health is quoted in the press as stating that he cannot see that it will do much harm, and it may possibly do some good.

D. E. H. CLEVELAND

### Manitoba

A combined meeting of the North-western District Society and the Brandon and Medical District Society was held at Clear Lake on September 9th. The principal speakers were Dr. Gordon Fahrni, of Winnipeg, and Dr. F. R. Bird, of Boissevain.

At the time of writing about 80 cases of anterior poliomyelitis have been reported this fall, chiefly from south-western Manitoba. The epidemic originated about Boissevain, and deaths have been reported from that town, Morden, and Portage la Prairie. Dr. M. R. Elliott, D.P.H., of the Department of Public Health, is working on the field and giving assistance to the local doctors. All the municipalities in which more than four or five cases have been reported have agreed to provide free diagnosis and treatment. Supplies of convalescent serum are being sent out as required from the provincial bacteriological laboratory at Winnipeg.

Dr. S. C. Peterson, Director of Social Diseases for the Manitoba Department of Health and Public Welfare, and clinical instructor in these diseases in the Faculty of Medicine, University of Manitoba, has resigned to become Director of Social Disease Control for British Columbia, and left on September 15th to assume his new duties.

On September 17th, at the Fort Garry Hotel, Winnipeg, a dinner was given in honour of Dr. R. G. Inkster, late Professor of Anatomy in the Faculty of Medicine, University of Manitoba, who will leave shortly to assume a position as Anatomist in Trinity College, Dublin. Dr. J. A. Gunn, Professor of Surgery, was in charge of the arrangements.

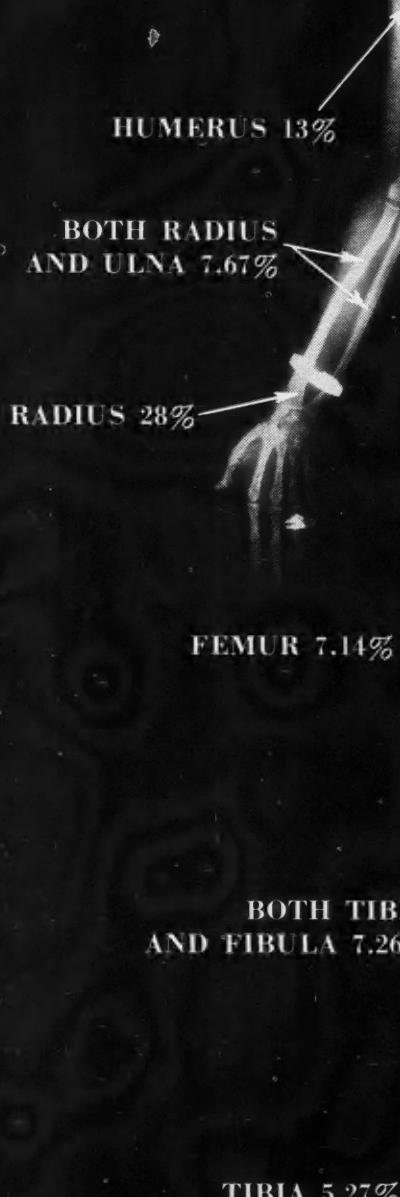
ROSS MITCHELL

### New Brunswick

Dr. S. S. Skinner has retired, as from September 1st, from the position he has held as chief medical officer of the Lancaster Hospital under the Department of Pensions and National Health. Dr. H. D. Reid, Federal Quarantine officer, at Partridge Island, Saint John, has been transferred to Lancaster Hospital to succeed him. Dr. Skinner has been identified with the Lancaster Military Hospital since 1919 and has been Medical Director of the Hospital since 1924. He was for many years an attending physician at the Saint John General Hospital. He served overseas, and his many friends wish him a pleasurable retirement.

Dr. C. O. McKay has been appointed assistant in the Department of Physical Medicine, at the Saint John General Hospital.

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Dr. A. L. Donovan, of the Department of Medicine at the Saint John General Hospital, has returned home following a month's post-graduate course at McGill University.

The program for the meeting of the New Brunswick Medical Society at Bathurst is complete. The scientific program includes both Maritime and Upper Canadian speakers. The North Shore Medical Society are hosts this year of the Parent Society.

Dr. D. C. Malcolm, Dr. V. D. Davidson, both of Saint John, and Dr. E. T. Kennedy, of Sussex, N.B., have returned from Europe, which they visited in connection with the Vimy Pilgrimage. A. STANLEY KIRKLAND

### Nova Scotia

The fifteenth session of the annual Dalhousie Refresher Course was held in Halifax, August 31st to September 1st, with a record attendance. Since its inception this post-graduate course, presented by the Medical Faculty of Dalhousie University and her associated hospitals, has grown in popularity with the Nova Scotia medical profession. This year it was held in conjunction with the annual meeting of the Nova Scotia Medical Society. The registration mounted to 183, of whom more than 100 were from outside Halifax. This was far in excess of the Medical Society registration. It represents about 40 per cent of those in active practice in the province! Than this figure no higher compliment could be paid both to the Refresher Course and to the profession that took advantage of it.

The program followed the general plan of previous years. The mornings were devoted largely to hospital clinics, conducted by staff members and guest clinicians; afternoons to lectures. Symposia, prominent features of the past two sessions, were omitted from this course, but through the week ran a theme, the subject of infant and maternal welfare. It has been the policy of the Refresher Course Committee to present informal addresses of a teaching nature rather than the more polished, but less engaging, presentation of manuscripts. This was carried out in every instance.

Dr. C. H. Best, of Toronto, told the story of protamine-insulin and its place in diabetic therapy. Dr. Channing Frothingham, Physician-in-Chief at the Faulkner Hospital, Boston, Mass., in two lectures, took up the "Organization of a community hospital for the best of service" and "The present status of endocrine therapy". Dr. Frothingham's first talk was of real value to those vitally interested in the many small hospitals throughout Nova Scotia. His refreshing conservatism in endocrine therapy was a tonic to many suffering from an inability to reconcile clinical results with drug agents' perorations.

Dr. J. H. Couch, Fellow in Surgery, University of Toronto, presented ingeniously and instructively a demonstration of local anaesthesia, Kirchner wire, and the walking cast in the treatment of fractures. As his second lecture Dr. Couch took up the injection treatment of varicose veins and haemorrhoids. Diagnosis and treatment of enlargements of the superficial lymph glands and, again, of conditions associated with jaundice were the subjects of Dr. Ray F. Farquharson, Professor of Therapeutics, Toronto University. Dr. Farquharson's presentations were lucid, practical and most comprehensive.

Maternal and infant welfare was considered in its many phases by Dr. A. L. MacLean, Epidemiologist of Dalhousie University, Dr. Atlee, Professor of Gynaecology, Dr. Maclellan, Professor of Obstetrics, and Dr. Wiswell, Associate Professor of Pediatrics. Dr. Johnston, Roentgenologist to the Victoria General Hospital, discussed, in two lectures, the principles and practice of radiation therapy. Dr. Muir, head of the Department of Anesthesia took up spinal and intravenous anaesthesia.

Clinics were presented by each of the services of the Victoria General Hospital, by the Children's Hospital Staff and the Staff of the Dalhousie Health Clinic. There were lectures and demonstrations by Dr. Ralph Smith's Department of Pathology. Special clinics were given by Dr. Frothingham and Dr. Farquharson.

The Refresher Course Committee with whom lay the responsibility for the planning and organization of the course consisted of Dr. Hugh W. Schwartz (chairman), Drs. T. M. Sieniewicz, N. H. Gosse, G. A. Winfield, Victor Mader, Gordon Wiswell, C. W. Holland, J. A. Noble, Ian Macdonald, and Dean Grant of the Medical School.

That the provincial government take full responsibility for the tuberculous sick of the province was the tenor of a resolution passed by the Union of Nova Scotia Municipalities at their annual meeting at Digby. The financial burden in the case of patients without means of support was, they felt, more than several of the municipalities could bear.

The annual golf tournament of the Nova Scotia Medical Society was won by Dr. P. A. MacDonald, of Halifax. Dr. J. W. Merritt, of Halifax, was low net, while Dr. W. G. Colwell, also of Halifax, had the unique glory of a hole in one.

Dr. C. J. W. Beckwith (Dal. '27), assistant superintendent of the Nova Scotia Sanitarium has gone to the University of Toronto, where he will spend the next year in the study of hygiene and public health.

Returning from two years' post-graduate work in New York, Dr. Carl F. Messenger, son of Dr. F. S. Messenger, will resume his practice in the Annapolis valley.

Senior among those registered at the Dalhousie Refresher Course was Dr. M. A. Curry, Professor of Obstetrics and Gynaecology at the Dalhousie Medical School from 1888 to 1921. Dr. Curry is active and well in his eightieth year.

Dr. B. F. Miller, New Waterford, has sailed for Europe where he will spend the next year in post-graduate study. Mrs. Miller and their young son accompany him.

ARTHUR L. MURPHY

### Ontario

Dr. Charles H. Gundry, who has been on the staff of the Toronto Psychiatric Hospital, has received a Commonwealth Fund Fellowship, which carries with it an appointment at the Child Guidance Clinic, Cleveland.

The Ontario Department of Health has issued a Bulletin notifying all municipalities that, after September 1st, they will have to pay 25 per cent of the cost of insulin supplied free to indigents.

Dr. E. L. Williams, of London, has been elected President, for 1936-1937, of the Medical Alumni of the University of Western Ontario.

Contracts totalling over \$25,000 have been let for the erection of a nurses' home at the Kitchener-Waterloo Hospital.

Professor H. B. Maitland, a graduate in medicine of the University of Toronto of 1916, and now of the University of Manchester, has been appointed Dean of the Medical School in succession to Professor H. S. Draper, who was, at one time, on the staff of the University of Toronto.

J. H. ELLIOTT

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### Quebec

It has been customary for the past few years to hold a St. Luke Day's Service in St. George's Church, Montreal. This service has been conducted by the rector, the Ven. Archdeacon Gower-Rees, who also preached the sermon. The lessons were read by medical men, usually by Dr. W. W. Francis, the late Dr. Campbell Howard, and Dr. Frank Patch, and other medical men acted as sidesmen. This year the service will be held on the morning of October 25th and will present a new feature in that a medical man will preach the sermon. Dr. G. N. Paterson-Smyth, the son of a former rector of the Church, will be the special preacher. His subject will be "Fear and Courage".

### Book Reviews

**The Practitioner's Library of Medicine and Surgery.**  
Vol. 10, Dermatology and Syphilology. 1043 pages, illustrated. Price \$10.00. D. Appleton-Century Co., New York and London, 1936.

The preceding nine volumes of this series were reviewed in the December, 1935, and June, 1936, issues of the *Journal*.

In the section of dermatology, the physical and mental constitutional habitus, the blood chemistry, and the occupation of the patient have been given more than usual consideration. In common with other works a good description of the anatomy and physiology of the skin is given. Diagnosis is approached from three angles, namely, the pathological, the specialistic, or area of distribution, and that of the general practitioner, or progress. There is up-to-date evaluation of the various drugs used, externally and internally. Enesol is recommended in lichen planus for its symptomatic and curative value. The use of the monopolar diathermy current is replacing to a large extent the use of caustics; x-ray treatments are given the prominence they deserve. Fungous infections, superficial and deep, are thoroughly handled; the importance of residual foci, such as onchomycosis, have not been generally accorded by public health authorities and others the prominence they warrant. The use of photographs of microscopic slides would have enhanced the practical value of this chapter. The roles of the calcium-potassium ratio of the blood serum, the pathological blood sugar curve and the blood uric acid content are stressed in the intertriginous and eczematous states. The Urbach proptone manner of diagnosing food hypersensitivity is given favour over the Vanderbilt Clinic Diets. The discussion of the seborrhoeic diathesis is indeed refreshing in this day of commercially-lauded but hopelessly ineffectual "antiseptic" treatment.

The section of syphilis is marked by the insistence on dark field examination as the primary requisition in diagnosis. In the author's opinion continuous treatment for the first year by an alternate series of ten injections each of arsphenamine, and a heavy metal gives the highest percentage of clinical and serological "radical cure". And, "in view of the frequency of relapse or progression in any stage of the infection, no syphilitic patient should ever be dismissed as cured". He attempts to define immunity to the *Treponema pallidum*, and in this regard he places pregnancy as the factor of greatest efficiency; early treatments, irregularly given, are the most harmful factor. They prevent the development of tissue response. His analysis of the Wassermann-fast state is stimulating. He would have all Wassermann tests made on the titration basis and base improvement by such. Wassermann "fastness" at the completion of six months of treatment means that ocular or neurosyphilis was present before treatment began, and our attempts should also be directed immediately to their arrest. This volume presents the 1936 analysis of dermatology and syphilology and should be of interest to every practitioner.

**Diseases of the Respiratory Tract.** By various authors. 418 pages, illustrated. Price \$6.25. W. B. Saunders, London and Philadelphia; McAinsh & Co., Toronto, 1936.

This volume covers a wide range of subjects in the field of respiratory diseases. It is a record of newer viewpoints in this important field as given in a series of lectures by outstanding authorities at the Eighth Annual Graduate Fortnight in New York. Among the subjects treated are Allergy in Relation to Respiratory Diseases; the Common Cold; Diseases of the Larynx; Trachea and Bronchi; Bronchoscopy; Pneumonia; Bronchiectasis; Pneumonocytosis; Tuberculosis; Emphysema and Carcinoma of the Lung. The discussion of the newer contributions to our knowledge in these fields is presented in a critical and very readable fashion.

The present status of allergy in relation to Hay Fever and Asthma, and the evaluation of skin tests is particularly well outlined by Ramirez. Jackson, in his usual lucid style, covers the field of bronchoscopy. Tuberculosis is discussed from the point of view of its evolution and immunity reactions as seen in the human individual at various ages. There are many valuable facts and much sage wisdom in these two chapters. The importance of the industrial hazard in relation to silica dust and its association with tuberculosis is discussed under pneumonocytosis by Gardner. Yandell Henderson has contributed an intriguing chapter on the physiological factors in massive collapse of the lung.

This is a book which can be profitably read and used for reference both by the internist and the general practitioner.

**The Common Cold and Influenza and their Relationship to other Infections in Man and Animals.**  
J. E. R. McDonagh, F.R.C.S. 148 pages. Price \$3.75. Wm. Heinemann, London; Macmillan, Toronto, 1936.

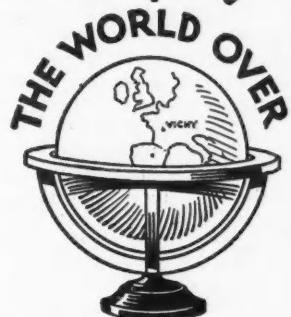
As the title indicates the author sets out in an attempt to correlate rather than differentiate various types of infectious disease. He develops the theory that *B. coli communis* in the intestinal tract is the common parent of a host of other organisms. These organisms, he believes, arise as mutation forms of *B. coli* and invade various regions of the body, causing a wide variety of infections including the common cold and influenza. The author does not accept the recent work on filterable viruses in the production of the latter diseases except in that the viruses are mutation forms of *B. coli communis*.

The book is certainly unorthodox, and one feels that few bacteriologists and epidemiologists will agree with the author's viewpoint. Dr. McDonagh is rather too dogmatic in his assertions and too far-reaching in his conclusions from the amount of clinical and experimental data presented. A perusal of this volume however gives one food for thought in the explanation of the factors which influence the incidence of epidemic disease.

**Exophthalmic Goitre and Its Medical Treatment.**  
Israel Bram, M.D., Medical Director, Bram Institute for Treatment of Goitre, Upland, Pa. Second edition, 456 pages, illustrated. Price \$7.00. C. V. Mosby, St. Louis; McAinsh & Co., Toronto, 1936.

In 1920 we had the pleasure of reviewing Dr. Bram's work, *Exophthalmic Goitre and Its Non-Surgical Treatment*, with favourable comment. Since that time the author has continued his interest in the subject, and with much more extensive experience and observation has written this volume, practically a new work. He makes it quite clear that he believes Graves' disease is not thyrogenous in origin, but is a neuroendocrine dysfunction, with or without hyperplasia of the thyroid gland, and that psychic trauma is the most evident provocative factor in its causation. His wide experience leads him to believe that thyroidectomy removes only a result of the disease, not the cause, and hence it only ameliorates the symptoms. He states the indications for thyroidectomy, but considers that they are present in only about 2 per cent of all patients. Toxic adenoma, clearly a neoplastic condition, requires surgical treatment, but this disease is not in-

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cluded. He discusses only Graves' disease. In his preface he says "The more competent the surgeon, the greater the emphasis on pre-operative and post-operative medical treatment as vital to the patient's welfare, until, when we examine the contributions of leaders in this field, we find skepticism respecting the adequacy of thyroidectomy in the average case of Graves' disease". He even suggests that the time has come for the profession to render obsolete the orthodoxy of an attack on the thyroid as a treatment of the disease. He reports that he has followed up 2,600 cases treated medically, and after three to twenty years he finds 90 per cent are entirely well. The remainder are relatively well, and most of the 10 per cent in this group are enjoying complete social and economic usefulness. Outside the section on treatment there is a full presentation of the various theories of the etiology of the disease, its symptomatology, diagnosis, types, laboratory tests, and a chapter on prevention.

**The Relief of Pain.** Harold Balme, M.D., F.R.C.S., D.P.H. 392 pages. Price 12s. 6d. J. & A. Churchill, London, 1936.

Some seventy-five years have passed since John Hilton delivered his famous lectures which in book form are a classic that all students and practitioners should read. Time had only served to emphasize the value of his observations upon rest as an essential factor in the relief of pain. In recent years investigation and observation, both clinical and experimental, have added to our knowledge of the nature of pain, its pathways, whether visceral or referred, and variations in sensitivity.

Dr. Balme emphasizes that the first essential in the treatment of pain is a knowledge of its cause. After a discussion of the nature of pain, its problems and investigation, he has practical chapters on prevention, on pain from inflammation and from injuries, and then proceeds to pain in the various systems, skeletal nervous and circulatory, before taking up the subject of regional pain and therapy, both general and local. There is a valuable chapter for ready reference, listing analgesic drugs with their composition, therapeutic use, and dosage.

He has assembled in a critical study the preparations and physical methods available for the prevention and alleviation of pain, indicating their limitations and dangers. Throughout there appears evidence of wide experience, as well as of keeping abreast of every advance in this special field of therapeutics.

#### Surgical Pathology of the Gastro-Intestinal Tract.

Arthur E. Hertzler, M.D., Surgeon to the Agnes Hertzler Memorial Hospital, Halstead, Kansas. 311 pages, illustrated. Price \$5.00. J. B. Lippincott, Philadelphia, Montreal, and London, 1936.

This is one of an ambitious series of monographs on surgical pathology, written by one of wide experience in pathology as well as surgery and gifted with a facile pen. His story is most readable. The illustrations are outstanding, not alone from their excellence but also on account of the very effective use of insets. Frequently the main illustration depicts a gross specimen, with an inset of either a low or high power view, or both, of the topical lesion. Each chapter gives the author's views in no uncertain terms. In dealing with the relationship between gastric ulcer and carcinoma, a definite stand is taken against their frequent association. The subject material is well arranged and fairly complete. That most interesting, though rare, condition, adenoma of the pancreas, might well have been included.

This book should be of practical value not only to the surgeon but also to the internist. It is more clinical than pathological.

**The Specificity of Serological Reactions.** Karl Landsteiner, M.D., The Rockefeller Institute for Medical Research, New York. 178 pages. Price \$4.00. C. C. Thomas, Springfield and Baltimore, 1936.

The author brings together in this review the most recent concept of the chemical aspects of immunological reactions. The material has been arranged in more or less the same sequence as the development of the subject.

There are five main chapters, dealing with (1) The Serological Specificity of Proteins, (2) The Specificity of Cell Antigens, (3) The Specificity of Antibodies, (4) Artificial Conjugated Antigens, and (5) Chemical Investigations on Specific Cell Substances; Carbohydrates, Lipoids. The author draws liberally from his vast experience in this subject, and also includes abundant references to other workers in this field. A perusal of this work outlines the important part the application of chemistry plays in the field of immunology. From a knowledge of the chemical constituents of the various antigens specificity of reactions is now readily explained. A very comprehensive bibliography is given at the end of each chapter, enabling ready reference to any part of the subject. The text lacks no element of detail and yet it is written in a most readable fashion. This is a review from the pen of one of the most conversant workers in the problems of this subject and may be highly recommended. The printing and binding are of the usual high order.

**Manual of Practical Obstetrics.** O'Donel Browne, M.B., B.Ch., B.A.O., F.R.C.P.I., L.M., M.C.O.G., Assistant Gynaecologist, Sir Patrick Dun's Hospital, Dublin. 363 pages, illustrated. Price \$6.00. John Wright & Sons, Bristol; Macmillan Co., Toronto, 1936.

The manual of practical obstetrics just been published by O'Donel Browne of Rotunda Hospital, Dublin, is a nicely bound, clearly written, well illustrated book. It is fashioned after Evans' Manual of Obstetrics, published in 1909, in that it is specially designed to suit the requirements of the undergraduate student and the general practitioner of medicine. The literature is well divided into chapters. The chapters upon normal labour, the toxæmias of pregnancy, puerperal sepsis, pelvimetry, and radiology in obstetrics contain a full description, concisely written. The chapters upon embryology or development, endocrine studies in obstetrics, development of the placenta, and the pathology of the placenta are too brief, and do not do justice to their importance in obstetrics. Posterior positions are also briefly dealt with, and many of the recent and valuable advances described in American literature are not mentioned. The book ends by giving an explanation of blood transfusion, and this, together with the subject of radiology in obstetrics, is new and of immense value. This publication can be highly recommended to the undergraduate student in medicine and also to the general practitioner, because many valuable points in the technique of obstetrics are emphasized.

**The Extra-ocular Muscles.** Luther C. Peter, A.M., M.D., Sc.D., Professor of Diseases of the Eye, University of Pennsylvania. Second edition, 351 pages, illustrated. Price \$4.50. Lea & Febiger, Philadelphia, 1936.

In this second edition Peter has followed the principles laid down in the first, so that the text has not been materially altered in fact or principle, though the advances of recent years have been included.

A chapter on operative technique has been added, and, whilst the author does not pretend to include all of the many excellent procedures of others, measures practised by himself and found to be satisfactory have been stressed. The book is well illustrated, and, as Peter from his vast experience in work of this kind can speak with authority, the book can be highly recommended.

**Post Mortems and Morbid Anatomy.** Theodore Shennan, M.D., F.R.C.S., Professor of Pathology, University of Aberdeen. Third edition, 716 pp., illustrated. Price \$9.00. E. Arnold & Co., London; Macmillan, Toronto, 1935.

The new edition of this splendid post-mortem reference book follows the same general outlines as the previous edition, beginning with a general statement concerning post-mortems, including a list of equipment. This is followed by a description of the performance of a post-mortem in great detail, including autopsy technique, and restoration. A scheme of examination of each organ and part of the body is presented and accompanied by a dis-

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cussion of the various diseases of the part in question. The discussion of medico-legal examinations and reports is very good. A very complete manual which could well be included in the equipment of every autopsy room and kept there for ready reference.

**Tuberculosis.** Gerald B. Webb, M.D. Clio Medica Series No. 16. 184 pages. Price \$2.00. Paul B. Hoeber, New York, 1936.

This pocket-size volume is the sixteenth in the popular Clio Medica series of primers on the History of Medicine. The author covers in a concise authoritative manner the development of our knowledge of tuberculosis. The division of the subject matter into chapters dealing with various phases of tuberculosis makes the volume particularly valuable. The subjects treated are contagion, pathology, bacteriology, immunity, and treatment in their historical aspects. The book contains much useful historical data cleverly woven into an easily readable story of this important disease. There are a number of interesting illustrations, and an extensive bibliography.

**Studies in the Psychology of Sex.** Havelock Ellis. Four volumes. Price \$16.00 the set. Random House, New York; Macmillan, Toronto, 1936.

This well-known and monumental work by Havelock Ellis, previously restricted in its sale, now appears in popular form for general consumption. The topics discussed are the following: Vol. 1—The Evolution of Modesty; Sexual Periodicity; Auto-erotism; Analysis of the Sexual Impulse; Love and Pain; The Sexual Impulse in Women. Vol. 2—Sexual Selection in Man; Sexual Inversion. Vol. 3—Erotic Symbolism; The Mechanism of Detumescence; The Psychic State in Pregnancy; Eonism and other Supplementary Studies. Vol. 4—Sex in Relation to Society.

The author, in a lengthy preface, details the history of his work and the vicissitudes which it met with until now, when the change in outlook and opinion has rendered it possible to present it without fear of active opposition. He regards sex "as the central problem of life" and believes that "the question of sex—with the racial questions that rest on it—stands before the coming generation as the chief problem for solution". This is the *raison d'être* for the book. Whatever one may think as to the necessity of popularizing (and vulgarizing) information of the kind given in the book, and, in our opinion, it is hardly edifying for non-professional readers, yet there can be no doubt that it is of great value to the physician, lawyer, sociologist, ethnologist, and educationist. The various subjects are dealt with in detail and with completeness, the arguments being supported by the testimony of physicians and patients, by case-reports and case-histories, and by quotations from poets, novelists and theologians. It would be hard to think of any point that has been overlooked.

**Principles and Practice of Recreational Therapy for the Mentally Ill.** John E. Davis, B.A., M.A., Senior Physical Director, Veterans' Administration Facility, Perry Point and William R. Dunton, Jr., Instructor in Psychiatry, The Johns Hopkins University, 197 pages. Price \$3.00. A. S. Barnes, New York, 1936.

The author defines recreational therapy as any free voluntary and expressive activity—motor, sensory, or mental, vitalized by the expansive play-spirit, sustained by deep-rooted pleasurable attitudes, and evoked by wholesome emotional release, prescribed by medical authority as an adjuvant in treatment.

Attempts to readjust mental patients are often frustrated by the intense preoccupation which the patient has with his own fantasies, delusional ideas, and feelings, which make it apparently impossible for him to become interested in the realities which surround him. Occupational therapy such as is outlined in this book is frequently exceedingly helpful in the attempts at re-education and re-socialization of these patients. This is well borne out by the favourable response of patients in those mental hospitals which have equipped themselves with facilities for recreational and occupational therapy.

After discussing briefly the various types and disease entities in this field, and indicating the major concepts involved in the process of re-education and re-socialization, the author proceeds to classify in considerable detail the various types of activities, formal and informal, exercises and games, which may be employed in this therapeutic endeavour with certain types of patients.

This book will certainly be a valuable aid to the physician who is specially interested in nervous and mental disease.

**Nursery Education, Theory and Practice.** William E. Blatz, M.A., M.B., Ph.D. and Dorothy Millichamp, M.A. and Margaret Fletcher, all of the St. George's School for Child Study, University of Toronto. 365 pages; price, \$3.50. Published by William Morrow and Co., New York, 1935.

Based chiefly upon their work at St. George's School for Child Study, the authors set out in a clear and logical manner the theory and methods used in the education of the young children under their care. The book is particularly satisfactory in that it gives not only the broad principles underlying the educational plan but also the detail of application. It is satisfactory to know that in Canada this most important subject of nursery schools is being studied, and that those directing the study are capable of passing on their experience in such a publication. Anyone who desires to have a definite guide in the training of young children will find it in this volume.

#### BOOKS RECEIVED

**On Percussion of the Chest.** Being a translation of Auenbrugger's Original Treatise. John Forbes, M.D. 31 pages. Price \$0.75. Johns Hopkins Press, Baltimore, 1936.

**Williams' Obstetrics.** Henricus J. Stander, M.D., F.A.C.S., Professor of Obstetrics and Gynaecology, Cornell University. Seventh edition, 1269 pages, illustrated. Price \$10.00. D. Appleton-Century, New York and London, 1936.

**The Vegetative Nervous System.** Wulf Sachs, M.D. 168 pages, illustrated. Price \$4.50. Cassell & Co., London; McAinch, Toronto, 1936.

**Heart Disease and Tuberculosis.** S. Adolphus Knopf, M.D., New York. 108 pages, illustrated. Price \$1.25. Livingston Press, Livingston, N.Y., 1936.

**Contraception\* as a Therapeutic Measure.** Bessie L. Moses, M.D. 106 pages. Price \$1.00. Williams & Wilkins, Baltimore, 1936.

**A Diabetic Manual.** Edward L. Bortz, A.B., M.D., F.A.C.P., Associate Professor of Medicine, University of Pennsylvania. 222 pages, illustrated. Price \$2.00. F. A. Davis, Philadelphia, 1936.

**Chemical Procedures for Clinical Laboratories.** Marjorie R. Mattice, A.B., Sc.M., Assistant Professor of Clinical Pathology, New York Post-Graduate Medical School of Columbia University. 520 pp., illustrated. Price \$6.50. Lea & Febiger, Philadelphia, 1936.

**Research on the Low Potencies of Homœopathy.** W. E. Boyd, M.A., M.D., Radiologist, Glasgow Homœopathic Hospital. 38 pages. Price \$0.75. Wm. Heinemann, London, 1936.

**Textbook of Pharmacognosy.** George E. Trease, B.P., Ph.C., F.L.S., Lecturer on Pharmacognosy, University College of Nottingham. Second edition, 671 pages, illustrated. Price \$6.25. Baillière, Tindall & Cox, London, 1936.

**Textbook of Neuro-Anatomy.** Albert Kuntz, Ph.D., M.D., Professor of Micro-Anatomy, St. Louis University School of Medicine. Second edition, 519 pages, illustrated. Price \$6.00. Lea & Febiger, Philadelphia, 1936.

